REMARKS ON TUBERCULIN THERAPY.

A Thesis submitted for the

M.D. Edinburgh.

by

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Introduction.

Tuberculosis and how to deal with it is the biggest medical, and social, problem of the present day throughout the civilized world. In England alone there are more than 55,000 deaths recorded each year, - more than 150 per diem. It is impossible to compute the morbidity, but it is certainly very high.

The economic cost is tremendous. It can probably be reckoned in millions of pounds sterling per annum.

Our present system of sanatoria are notoriously unsatisfactory, chiefly because patients are not able to remain in residence a sufficiently long time, but also because when they are discharged they are unable to lead the hygienic life to which they were accustomed when under treatment. Consequently, in many instances, they rapidly go back to their previous state of health. Even where a cure is effected by sanatorium treatment, which one must

concede is the case in many instances, it still has the grave defect that the patient whilst an inmate ceases to be a wage earner.

It is unnecessary to apologise, therefore, for dealing in the present thesis with the present position of the Tuberculin treatment of tuberculosis.

Robert Koch discovered the tubercle bacillus in 1882. Shortly after this he introduced Tuberculin, which he considered has a specific action upon the tubercle bacillus. It was soon found, however, that Tuberculin is a very dangerous weapon if used indiscriminately. Too large doses were given in advanced cases, against Koch's solemn warning, with disastrous results. Virchow, in particular, reported most unfavourably on the treatment, and Tuberculin received, what to most appeared to be, its death blow.

A small number of earnest workers, however, impressed with the brilliant results occasionally attained, even in these early days, felt that there must be value in Tuberculin and that the fault lay, not in the remedy, but in the manner of using it. They soon realised that the dose as originally given was far too big. Notable amongst these "die-hards" was Sir Almroth Wright, who, working at the "opsonins" of the blood plasma, was able to prove that the opsonic index could be raised by small, and increasing, doses of Tuberculin.

All workers who have had extensive experience of Tuberculin are convinced of its value. They differ, however, in their mode of administrating it, and the theories they hold regarding its action also differ.

I propose, therefore, to give a review of the present position of Tuberculin Therapy from a study of recorded literature, and to describe my own experience in the treatment of a series of cases.

HISTORICAL OUTLINE.

I now propose to indicate shortly the main work that has been done on Tuberculin since its discovery up to the present time. In 1882 Koch proved the tubercle bacillus to be the cause of tuberculosis. Shortly after this he began to experiment on guinea pigs with sterilized cultures of tubercle bacilli. He found that after infection with tubercle bacilli a second infection had no hold, proving that the first infection had established a degree of immunity. He further proved that infection into a healthy guinea pig produced no effect except local suppuration, but that if a tubercular guinea pig were infected, that guinea died unless minute doses were used. Their lives could, however, be saved and their condition of health improved if high dilutions of the emulsion were used. It was found that these emulsified bacilli were not absorbed but gave rise to a local abscess. This proved that the curative substance must be dissolved out of the

bacillus. The attempt to extract this curative agent led Koch to the discovery of Tuberculin. He published his results in 1890, and pointed out that Tuberculin does not kill the bacilli, but causes necrosis of the living tubercular tissues.

He noted the improvement that took place in early phthisis and that cases were cured, apparently, in a month to six weeks. He amphasised the importance of early treatment, and deprecated the use of Tuberculin in advanced cases, and pointed out the dangers of mixed infection.

A year later Ehrlich, and other workers in Koch's Institute, started a mild method of innoculation, commencing with minute, but gradually increasing doses. This system is used by many at the present day. In 1891 Hetweg wrote a paper to the effect that Tuberculin exercised a positive chemiotactic action on the leucocytes leading to a focal reaction.

About this time Von Pirquet introduced his subcutaneous test for diagnostic purposes. He scarified the epidermis of the forearm and applied a drop of Old Tuberculin. In 24 to 48 hours the spot in the tubercular became inflamed; in the non-tubercular there was no change in the part.

This test has, to a great extent, been given up as it was too delicate. The great majority of adults react to it.

It has, however, been re-introduced in a modified form. Old Tuberculin is still used, but diluted to 1 in 10; 1 in 100; 1 in 500. A reaction to 1 in 500 points to active tuberculosis, in a lesser degree 1 in 100, and 1 in 10 point to activity. The test so modified is useful, but its value depends upon the skill of the interpreter.

In 1901 Koch introduced the intra venus method of innoculation as the agglutinating power could be raised higher, but this proceedure soon dropped out of favour.

In 1901 Goetsch introduced the reactionless method which had previously been advocated by Petruschky and others. It has the following advantages, as pointed out by Bandaleir and Roepke:

1. It is harmless.
2. Although minute doses are used at the beginning, high and powerful doses arentually are able to be given.
3. It enables Tuberculin to be used in severe cases.
4. It is no bar to the patient remaining at work.

About the same time Petrushky advocated interrupted treatment; two or three months treatment and then an interval of rest for a like period. The method is apparently a good one, but the difficulty of getting people to return

for further courses is a great drawback.

Very important work was published by Wright in 1903. Working at his opsonic index of the serum he found a period of intoxication varying with the amount of vaccine administered, during which the anti-bacterial power of the blood was reduced. This he called the "negative phase". After this negative phase the bacteridal power of the blood was increased: this he called the "positive phase". It lasts about a month. He considers, therefore, that frequent injections of Tuberculin are useless and that they increase the negative phase but not the positive.

In 1904 Lowenstein and Rappopat produced hyper sensibility by repeated small doses.

In 1906 Wassermann propounded a theory as to the presence or absence of the tuberculin reaction. By means of the "compliment fixation" test he proved the presence of dissolved products of metabolism of the tubercle bacilli, and of their anti bodies. These anti bodies, by combining with antigen, extract all the tuberculin injected from the blood and concentrate at the tubercular focus. As Tuberculin unites with anti-Tuberculin the compliment is fixed, hence there is an increase of lenescyte ferments in the tubercular focus leading to softening of the tubercular tissues.

In 1908 this was confirmed by Christian and Rosenblat.

Bauer, working at the compliment fixation test in children, found that if there was a fair amount of anti-tuberculin in the blood the reactions were slight.

In 1904 lung infusion was introduced by Jacob. His object was to bring the Tuberculin into close contact with the bacilli in the affected area. The method is, however, based on a fallacy. He did not realise that the Tuberculin is rapidly carried away from the diseased area and that it may do harm by damage to cell life. Oral administration, as recommended by Fregnoth is useless, as Tuberculin is not absorbed by the alimentary canal.

Carl Spengler advocated cutaneous innunction as being most suitable for weakly patients with fever. It has not been much used, but is strongly advocated by some, especially recently, notably by Sir Robert Philip.

Marmorek in 1906 stated that Tuberculin is not the toxin of the Tubercle Bacillus, but that it stimulates the recipient to manufacture another toxin in larger amount. He considered that there are two stages of the Tubercle Bacillus and that the products vary with the culture medium, and he thought that the production of the true Tubercle Bacillus toxin is greatest from what he calls primitive bacilli. He grew these on lencotoxic serum and extract of liver tissue. Marmorek's serum differs from Koch's Tuberculin in that it acts on other toxins of the

Tubercle Bacillus besides Tuberculin. He has, apparently, obtained good results himself, but in the hands of others the evidence of its value is conflicting.

In 1906 Sahli advocated very small doses continued for several years. He does not aim at immunity, but only at an immunizing curative effect.

In 1808 Neufeld concluded that the fact that opsonins are formed proves that the Tuberculin reaction is specific, but that the opsonins are the immunizing substance.

In the same year Turban and Baer considered that the small dose at long intervals, as recommended by Wright, produces little effect and tends to establish hyper-sensibility.

About this time Lowenstein, working on phagocytosis, noted intra cellular grouping of Bacilli in the lenescytes of the sputum.

In 1909 Pielhart proved that patients whose disease takes a favourable course possess a raised natural resistance to Tuberculin and that true anti toxins occur in the blood of Tuberculin treated patients. He recommended the administration of large doses of Tuberculin to be given at 14 day intervals, so as to maintain the quantity of anti bodies at a high level. He also tested Tuberculin immunity by means of mixtures of T.B. Serum. He proved that the serum of people with pulmonary tuberculosis not treated with Tuberculin and doing

very well, possess the same Tuberculin neutralizing bodies as the serum of patients treated with Tuberculin. In other words, Tuberculin imitates the natural cure.

In 1910 Rolly gave the results of 200 patients treated with minute doses. He proved that they produced hyper sensibility.

Penzolt later advocated large doses cautiously increased.

Citron assumed that there are toxic sensitive cells which, by the injection of small quantities of Tuberculin, become rich in receptors, and these attract the Tuberculin and produce the reaction.

Sahli considered the lysenized Tuberculin to be an active antigen.

Jochmann, the same year, recommended stopping treatment when no signs of reaction occurred and on subsequently testing, if a reaction occurred, he advised further treatment.

In 1911 Engel introduced a modification of Von Pirquet's reaction, using the dilutions as previously noted in this paper.

Mention must be made in passing of Calmettes opthalmic reaction.

3.

THE VARIETIES OF TUBERCULIN.

I now propose to give a brief resume of the principle Tuberculins, commenting on any of those of which I have personal experience.

We must first of all distinguish between those in which the aim is to produce an active immunity, and those in which passive immunization is sought.

By active immunization we mean "the changes in the organism which are the result of absorbtion of bacteria, or their products, and which lead to the appearance of specific protective bodies (anti bodies) in the serum." By passive immunization is meant "the production of immunity by means of a specific serum."

A. Preparations Intended to Produce Active Immunity.

1. Old Tuberculin (O.T.) Koch's original preparation.

Pure cultures of Tubercle Bacilli are grown on 5% glycerine broth, are sterilized by steaming, and concentrated to one-tenth its volume. The liquid is then separated from the bacilli by filtering. Old Tuberculin contains the

soluble secretions (toxins) in 50% glycerine dilution. It also contains the constituents of the bodies of the bacilli (endotoxins) which have been extracted by the above mentioned process.

Old Tuberculin is used by most advocates of Tuberculin for diagnostic purposes. It is not so much used for purposes of treatment as formerly. I used it extensively myself at one time, but have given it up in favour of T.A.F. (Tuberculin albusnose frei) as this produces less local reactions.

2. T.O.A. (Tuberculin original alt).

This is a filtered culture of human tubercle Bacilli not concentrated by boiling, and without the bacillary bodies. That is to say it contains the toxins but not the endo-toxins. It is ten times weaker than Old Tuberculin. Compared with Old Tuberculin it is less toxic, but according to Bandalier and Roepke, it is in no way superior.

3. P.T. Bovine Old Tuberculin.

This is prepared much as Old Tuberculin but from Bovine Bacilli. It is about five times weaker than Old Tuberculin. I used this extensively at one time. It sometimes causes very severe reactions and I have now given it up entirely.

4. P.T.O. This is a similar preparation to the last, but fifty times weaker. It is used chiefly as a preliminary to P.T. and O.T.

The system which Camae Wilkinson employed for many years was to start with P.T.O., then proceed to P.T., and end up with O.T. This is a cumbersome method, and a far more satisfactory way is to use one preparation only, such as T.A.F., throughout.

5. T.A.FC (Tuberculin albumose frei.)

The object of this preparation is to avoid the risk of anaphyllaxis, which might be established by the albumose. It is prepared as follows:
An albumose frei culture media is innoculated with a pure culture of human tubercle bacilli and incubated, and the volume is reduced to one-tenth of its original quantity. The bacilli are then killed by heat and separated from the culture medium by filtration. It corresponds to Koch's Old Tuberculin.

Bandelier and Roepke consider that it is better tolerated than Old Tuberculin, probably due to the absence of albumose. This I can confirm from personal experience. They state that as an anti pyretic it is far inferior to Bacillary Emulsion.

6. New Tuberculin. (T.R.)

The object of this preparation is to immunize the patient not only against the toxins, which is the role of Old Tuberculin, but also to kill the bacteria themselves as a typhoid vaccine does. Koch aimed at the absorbtion of as many bacilli as is

possible. The only way he found he was able to do this was by calling in the aid of chemistry. He made an extract of the Bacilli with a deci normal soda solution. This he called T.A., but this preparation caused abscesses, so Koch obtained a total disintegration of the Bacilli by rubbing up a desiccated culture in a mortar. This powder was then mixed with normal salt solution and centrifugalized into two layers. The upper one, T.O., resembles T.A., and contains the glycerine soluble substances. The lower layer is T.R., and contains the substances remaining after glycerine extraction.

Koch proved by experiments, on man and animals, that T.R., has immunizing properties. He found that he could produce the immunization without reactions. The point is to desensitize the patient to T.R., and at the same time to the Tubercle Bacillus. A patient immunized against T.R., will not react to O.T., and so is immunized against all the constituents of the Bacillus.

Bandelier and Roepke state that T.R. must not be used in advanced phthisis, but they say that in all other cases it is far superior to O.T., and allied preparations.

Koch advocated beginning with .0002 cc., and slowly increasing so as to avoid reactions. Owing to its low toxicity it is suitable for use in sensitive cases. The two great objections to its use are its high cost and its

liability to deteriorate.

7. New Tuberculin Emulsion (B.E.)

Koch found that he got better results by not separating T.O., from T.R., he considered that the best effect was obtained by rapidly increasing doses and marked reactions. Howevdr, he modified his views later and gave this emulsion in more gradually increasing doses and this is the plan now generally adopted. The initial dose is usually .0001 cc.

Bandelier and Roepke point out that B.E., has a more powerful antipyretic action than other Tuberculins.

7a. Sensitized Bacillary Emulsion (S.B.E.)

This was introduced by Meyer. It is prepared with a high valued tubercular serum which by its anti tuberculin is intended to destroy the toxin of the Tubercle Bacilli.

Citron considers that the injection produces less fever than other methods, but Bandelier and Roepke think, that though it is a good preparation, it has no special advantage over B.E. Moreover, it is a costly Tuberculin.

8. Landmann's Tuberculol.

This is a normal saline extract of highly virulent fat free Bacilli fractionally distilled. Landmann lays stress on bringing the patients to a high degree of immunity and keeping them there. It is, apparently,a very good preparation.

9. Tuberculoidin.

Klebs considers that there is a harmful toxin in Tuberculin

besides the curative agent, and that this could be separated by treating it with bismuth and alcohol. He further adds Pfeiffer's catarrhalis bacillus to combat the mixed infection. The preparation is given intra orally. It is harmless, but probably useless.

10. Beranack's Tuberculin. (T.B.K.)

This preparation is said to contain all the immunizing substances without the harmful toxins. It consists essentially of extra cellular toxins and of intra cellular toxins. Sahli considers it superior to all Tuberculins, but this is by no means the universal opinion.

11. Spengler holds the view that Bovine Tuberculin has far better immunizing powers against Human Tuberculosis than Human Tuberculin: consequently he introduced P.T.O., and P.T., referred to previously in these pages. It cannot be said that general opinion is in favour of these preparations. In my own practice I have discarded them for some time. They tend, I find, to give more severe reactions than T.A.F., without producing more favourable results.

12. Autogenous Vaccines.

Krause introduced these, holding that each patient had his own particular strain of Bacillus. The results do not seem to be superior to those obtained with stock Tuberculins.

13. Mixed Tuberculins.

These were introduced by Rothschild. These are a

mixture of various Tuberculins. He got good results, but they do not seem to be superior to those attained by ordinary preparations.

14. Mention must be made of Deny's Tuberculin, which is prepared by filtration through porcelain. He claims that as he avoids boiling there is no destruction of useful toxins. It is, apparently, in no way superior in its results to Old Tuberculin.

15. Rosenbach introduced a Tuberculin grown on a trichophyton medium. It is, apparently, a case of weakened tubercular action. It has been employed in surgical Tuberculosis, being injected where possible into the infected focus. Opinion as to its utility is conflicting.

15. Reference must be made to the combination of Tuberculin with such drugs as arsenic, iron, and iodine. This method does not seem to be much in vogue at present.

16. Nastin; Deycke, and Reschad Bey, working on leprosy, proved that the lepra Bacillus owed its specificity to a fat in the bodies of the Bacilli. This they called Nastin. They found that this fat, when injected into tubercular subjects, produced a severe reaction. On non-tubercular people no reaction occurred. Later, Deycke isolated a neutral fat analogous to Nastin which he named Tuberculo-Nastin. Good results have been obtained but it is somewhat dangerous on account of its bacteriolytic action.

B. Preparations Intended to Produce Passive Immunity.

1. Moragliano's Serum.

Moragliano considered that all the changes in the body produced by tuberculosis were due to the toxins, and that these toxins favoured the spread of the Tubercle Bacillus in the body. The body fluids possess anti-toxic, anti-bacterial, and agglutinating powers and that the serum contains therefore curative powers. To obtain this serum he injected into animals a filtrate of young and active tubercle bacilli, and a watery extract of dead bacilli. In other words, he used both the toxins and the bacilli. Evidence as to the value of this serum is conflicting, but on the whole it appears to be favourable.

2. Marmorek's Anti-Tubercular Serum.

Marmorek considered that there are two stages of the Tubercle Bacillus and different secretory products which depended on the variety of culture medium used. First there is the production of the true tubercle Bacillus toxin, which are chiefly the product of what he calls "Primitive Bacilli" These he grows on a "lenco toxic" serum and liver extract. He assumed that the presence of lencocytes stimulates the production of toxin, and that the liver extract retards the growth of the Bacilli which retain their primitive character. This primitive toxin differs from Koch's

Tuberculin in that the latter only produces anti tuberculin and has no effect on the other toxins of the tubercle Bacillus, whereas Marmorek claims that his serum produces immunity against all tubercular toxins. Marmorek himself seems to have had most favourable results, but the general evidence of others seems to be somewhat conflicting.

3. Hoechst Tubercular Serum. He worked on the assumption that, as Tuberculin only acts on tubercular subjects, the serum should be drawn from tubercular animals. Consequently, cattle, horses and mules, were infected by injecting with live Tubercle Bacilli and the serum of these animals utilized. This serum has not been generally used, but it is being reported upon favourably.

4. Streptococecus Sera. Denys and Van der Velde use a polyvalent serum for the purpose of attacking the mixed infection.

C. Vaccine Treatment.

This was first introduced by Wright who based his dosage on observation of the opsonic index. Its aim is to deal with the mixed infection. I myself have been in the habit of treating cases of obvious mixed infection with a detoxicated polyvalent vaccine added to Tuberculin. It seems to have a very favourable action on the catarrh and produces no rises of temperature, or other unfavourable symptoms.

D. Carl Spengler's Treatment with Human Blood (I.K.).

Carl Spengler considers that the red blood cells are the source of the protective substances in infective diseases, and especially in Tuberculosis. His preparation is obtained from the blood of rabbits which have been immunized against human tubercle Bacilli. Spengler reports that his preparation has powerful antipyretic properties and that it can be safely used in the worst cases of phthisis.

Bandelier and Roepke worked with this preparation for fifteen months and came to the conclusion that it was harmless but useless.

E. Detoxicated Vaccines.

Raw, B.M.J., Ap. 23. 1921. Emphasises the fact that human and bovine tuberculoses are antagonistic and that the two varieties cannot exist in the body at the same time, and that you can provide immunity against the human Bacillus by innoculating with Bovine Bacilli, and vice versa. He accordingly uses an attenuated virus of both varieties, which he obtains from subcultures of virulent Bacilli. He considers that these attenuated Bacilli are of value, not only for therapeutic, but also for prophyllactic purposes. It is questionable, in my opinion, whether by this means real immunity is obtained. My only experience, however, is of one case of enlarged abdominal glands, in an officer who was treated with

a full course of Raw's vaccine. He improved for a time but went back again. He was tested at Margaret Street Hospital for Consumption, and reacted to a modified Von Pirquet of 1 in 100 dilution of O.T. He was then sent to me for purposes of treatment. He was very sensitive at first to small doses of T.A.F., but later established tolerance. I fancy that Raw's vaccine is too attenuated and I believe that now he is using much bigger doses than formerly.

The Mode of Action of Tuberculin.

A very clear account of this is given in Sahli's "Tuberculin Treatment" and in this section I propose dealing with the theories therein propounded, criticizing them as far as my experience of the subject permits.

Tuberculin is practically inert in the non-tubercular, but in the tubercular subject it is powerful indeed, even in minute doses. How it acts was at one time a mystery, but the riddle is gradually being solved and we are now much nearer the truth than in the early days of its discovery by Koch.

Its Chemical Nature.

Sahli considers that in their chemical nature all Tuberculins are practically the same. He states that good results can be obtained from all Tuberculins, provided the right technique is employed, and that the search for new Tuberculins, in the hope that efficiency will be gained thereby, is futile. He believes in Beraneck's Tuberculin, Bandelier and Roepke's Bacillary Emulsion, Camae Wilkinson, formerly in P.T.O., and P.T., and O.T., (now I think he inclines to T.A.F.). For my own part I prefer T.A.F., for reasons previously stated, but

there is little doubt that Sahli is correct. It is not so much the preparation used that matters as the man who uses it, and the way he uses it. Pottinger, (Clinical Tuberculosis,) maintains that two men using the same tuberculin, in the same way, will not get the same results. In other words, the personal equation must be considered. Dr Harry Campbell tells me that suggestion ffequently plays a great part. In other words, the psychical side must be considered. Granting the force of this argument it can easily be refuted, as far as reactions are concerned, by giving an injection of salt solution without tuberculin, as I have often done. The result is invariably negative. According to some, there is little doubt that the active principle of all tuberculins is the same. The chief exponents of this view are Wolff-Eisner and Meissen. Others consider that the true tubercle toxin has yet to be discovered, basing their conclusions on the fact that up to now complete immunization of animals has not been accomplished. Others see essential differences in the varieties of tuberculin and, therefore, are always trying new varieties in the hope of ultimately reaching the perfect tuberculin.

That there is a common factor for all tuberculins is proved by the phenomena of the tuberculin reactions which are similar whatever tuberculin is used. The only difference is in the degree of the reaction.

Another proof is that the Tuberculin reaction is produced by B.E., (Bacillary Emulsion) which consists practically of nothing but ground up Tubercle Bacilli. In other words, the active principle is an endotoxin. A further proof is that by von Pirquet's cutaneous test and in the conjunctival test the tuberculous tissue can be produced. Jadassohn assumed that the tuberculous tissue was produced by ultra-microscopic particles of Tubercle Bacilli, which accounts for the local reaction. Zieler, however, proved that the same local tubercular processes could be produced by dialized tuberculin, but this is not at variance with Jadassohn's theory, as, according to present views on colloidal chemistry, in every albumen solution there are moleculor particles which have been revealed by the ultra microscope. Sahli works on the assumption that all tuberculins have the same chemical nature, for the reasons given above, and this seems to be sound argument, and the reactions are due to Tuberculin endotoxin. It follows the general law of the toxicity of foreign proteins. Tuberculin has, however, a very special action which is brought out by the following facts.

A. Quite large doses, say, .25 of A CC of Old Tuberculin can be tolerated in the non-tubercular.

B. It is extraordinarily toxic to the tubercular, even in the minutest doses. There are many explanations for these phenomena.

1. Tuberculin being the true chemical tubercle toxin, the

addition of this to that already in the body of the tubercular produces the general reaction, whilst its additions to the toxins already in the foci causes focal reactions. Wolff Eisner objects to this theory, pointing out that repeated very small doses will cause reactions even though the sum total dose is quite insufficient to cause a reaction. It is, moreover, not clear why a minute dose in latent tuberculosis, on occasion, will give rise to disturbance. Assuming, with Koch, that the healthy will react to 10 mgrms of Old Tuberculin, it is improbable that in latent tuberculosis a reaction to 1 mgrm will take place just because the amount added brings the total tuberculin in the body up to 10 mgms. It is illogical to suppose that all those who react to 1 mgm have 9 mgms already in the body. Some might contain only 1 mgm., and others 20. In the former several mgms would be required, in the latter only 1mgm., and it cannot be supposed that this is the case. So summation is not sufficient explanation.

2. What Sahli calls the "difference theory" is the opposite of the "summation theory" just dealt with. In this Difference Theory, presumed that the healthy body contains tuberculin anti toxin, when a small quantity of tuberculin is injected it is neutralized by the anti toxin and no reaction takes place. It must be assumed that in active tuberculosis there

is no excess of anti toxin; therefore, very small doses of Tuberculin produce reaction by summation. In latent tuberculosis there is a balance between the Tuberculin and the anti toxin in the body leading to reactions after small doses. This theory would explain why severe acute cases of tuberculosis fail to react to Tuberculin. The assumption being that the body is already so full of Tuberculin that the small additional dose given fails to cause a reaction.

This theory shows that the result of injections depends upon the relative amount of Tuberculin and anti toxin in the body. It, however, does not explain the incubation period, nor does it give any proof of the large amount of anti toxin which it assums to be present in the healthy body.

Pickert and Löwenstein took up this question. They made cutaneous injections into a healthy subject of their own Serum and Tuberculin, with the result that they still got a reaction and they could discovef no neutralizing action of the Serum on the Tuberculin. They were able to show, however, that in the tubercular who are doing well there are such neutralizing anti-toxic substances, and also in patients treated with Tuberculin, This is not in harmony with the Difference Theory, which demands a greater power to react in the healthy, than in favourable cases of tuberculosis.

3. The "Tuberculin Sensitive" theory. In this one assumes an innate sensitiveness in certain individuals, and that these people are generally tubercular is known to be correct. Firstly, because guinea pigs, who are very susceptible to tuberculosis, are very insensitive to Tuberculin unless they are tubercular, and secondly, Von Pirquet's reaction on infants produces very slight reactions proving that Tubercular sensitiveness is not innate, but is only present after injection.

4. Hertwig's Theory. He considered that the primary factor was the focal reaction and that this was the cause of the fever. He thought that the inflammatory process depended on chemiotactec actions. He considered that after an injection of Tuberculin the lencocytes became tolerant to the Bacillary toxin and that the concentration of the tubercle toxin in the foci has a positive chemiotactic action on the leucocytes, an action which was previously negative. Objection to this theory theory is taken in that it affords no explanation of inflammatory hyperaemia. It gives no explanation of fever without reaction in visible tubercular foci. Thirdly, it pre-supposes that the injected Tuberculin remains for some time in the blood, which Wolff-Eisner has proved not to be the case.

5. Wassermann and Brusk's Theory. By means of the "Compliment Fixation Test" they have found in the serum of patients

treated with Tuberculin a substance they call anti tuberculin. This substance with the Tuberculin causes absorbtion of compliment. A similar substance together with Tuberculin has been found in Tubercular foci. They conclude from this that focal reactions are the result of the fixation of the compliment which depends on the meeting of Tuberculin with anti tuberculin. As the result of this compliment fixation there is a softening of the tissues after Tuberculin injections, dependent on the digestive power of the compliment. If, however, the blood contains free ante tuberculin, as in the case of a patient treated with Tuberculin, the Tuberculin injected is neutralized and consequently has no effect on the tubercular focus. They consider that the general reaction is dependent on the focal, and they explain the inertness of Tuberculin in the case of the healthy by the fact that the latter have no anti tuberculin and no tubercular foci. They consider that anti tuberculin is a bacteriolytic amboceptor.

There are several objections to this explanation of the Tuberculin Reaction. For instance, it is not clear how Tuberculin and anti tuberculin can exist in the same focus without neutralizing each other under the action of compliment. It is difficult to understand how the meeting of Tuberculin and ante tuberculin can produce liquifaction of tubercular tissues. If we agree with Ehrlich's views on digestive

ferments, this digestive action would be mainly directed to the combination of Tuberculin and anti-Tuberculin. They further assert that this combination has a harmful focal action, but a de-toxic action on the blood.

6. Wollf-Eisner's Theory. Wolff-Eisner considers that the Tuberculin action is due to the presence of an anti body which is of the nature of amboceptor. He believes that Tuberculin is a foreign albuminous substance of low toxicity. It, however, becomes much more toxic when it comes in contact with a specific lysin and becomes lysinized. A tubercular patient contains tuberculysin in his body and so displays reactions as a result of lytic action, whereas the healthy person does not.

Sahli gives the following explanation of the focal reaction:

As a result of Tuberculin injection there is an acute lytic action in the foci, resulting in inflammation and temporary damage.

A more probable explanation is that the Tuberculin, after lysinization, is converted into a highly toxic substance which, in addition to fever, causes irritation of the tubercular foci. Wolff-Eisner's view, briefly, then is that reactions, local, focal, and general, are due, not to the Tuberculin itself, but to the product of a lytic anti

body on the Tuberculin. Sahli refers to this as Lysinized Tuberculin.

Von Piquet considers that Tuberculin action is due to anti bodies. His view is essentially different from that of Wolff-Eisner. The latter considers the action is a chemical one; the former that the action of the foreign albumen (Tuberculin), and its anti body act conjointly, in the same way as in serum disease. This theory is not so clear as that of Wolff-Eisner, since the latter, applying the analogy of bacterio-lysin to unformed albumen, assumes that hypersensitiveness is the result of a toxin substance due to the action of a lysin on the foreign albumen.

Sahli, who is a believer in the Lysin Theory, gives the following points as arguments in its favour:

1. It harmonises with the idea that Tuberculin is simply tubercle-bacillary protein, so that the comparison of Tuberculin reactions with hypersensitiveness in serum disease is plausible.
2. It is a known fact that in the digestion of albuminous bodies the products are more toxic than the original albumen. The Lysin Theory is compatible with this.
3. It explains why healthy mammals do not react to Tuberculin, the reason being that there are no tubercle bacilli, and so lysin is not produced.

4. It explains the incubation period of the reaction, the length of the incubation period depending on the amount of lysin formed.

5. It explains focal and general reactions, the former being due to the irritant action of the lysinized Tuberculin on the foci, the latter due to the general action of the lysinized Tuberculin in the circulation.

6. It explains why the sharper reactions do harm to the tissues which cannot be produced by non-lysinized Tuberculin.

7. Beraneck found that if the serum of a horse treated with his Tuberculin was injected into a tubercular guinea-pig the lethal danger was lessened but the thermal action of the Tuberculin was increased.

This harmonizes with the theory that the serum contains Tuberculinolysin which frees the fever producing substances more quickly and in greater quantity than Tuberculin without the serum, and the anti toxic content of the serum confines the bad effect of the Tuberculin simply to the production of fever.

Yamanouchi and Bauer, working on similar lines, found that under certain conditions Tuberculin sensitiveness can be transferred by a serum.

Nicolle Gay Southerd and Otto, found that this hyper sensitiveness to a foreign serum can be passively transferred

to normal animals in the serum of previously treated animals. These experiments expose the fact that hyper sensitiveness after injection of lysin containing serum only occurs after some hours or longer. The explanation is that the lytic anti body is an ambocæptor and that it cannot act until it has absorbed the compliment.

The essential feature of the lysin theory is that the action is a chemical one and that physical breaking up of the Baccili is quite secondary.

Sahli considers that hyper sensitiveness to Tuberculin and living Tubercle Bacilli is due to the large amount of Lysin in the blood of the patient and as a result large quantities of Tuberculin are lysinized and a powerful toxin is set free. He states, however, that this lysin theory cannot be really proved until Tuberculin sensitiveness has been passively transferred by the serum of Tuberculin sensitive animals. Yamanouchi and Bauer and Beraneck claim to have done se, but their experiments require verification. Supposing subsequent experiments prove the impossibility of passive transference then hyper sensitiveness could be explained as a kind of histogenesis, similar to the hypersensitiveness found in horses employed in the manufacture of tetanus serum. According to this theory the reactions would be the result of histogenous hyper-sensitiveness, caused by Tuberculin, not by lysinized Tuberculin. Tuberculin

would then only be toxic in patients who are hyper-sensitive. Sahli considers that this explanation is possible, and it certainly seems to fit in with practical experience, for when once one has overcome hypersensitiveness - provided one is able to do so - the patients who are victims of it seem to do very well on Tuberculin. This is very well seen in cases of Surgical Tuberculosis who often show marked hyper-sensitiveness to Tuberculin and yet are usually in better bodily health than those in whom the lungs are affected. As Sahli says, hyper-sensitiveness is a means of defence.

If this theory be correct the aim of Tuberculin treatment is to increase the histogenous defensive reactions and thus the anti toxins.

Theory of Tuberculin Diagnosis.

If the Lysin Theory be correct all the different tests subcutaneous, cutaneous, conjunctional, can be employed for diagnostic purposes. They all depend on the lysin produced by the action of Tuberculin on Tubercular infections and to the hyper-sensitiveness of the tissues to Tuberculin. The reason why Tuberculin is not always satisfactory as a diagnostic agent is because we do not directly diagnose tuberculosis, but the lysin-content, or hyper-sensitiveness. You may, therefore, get a positive reaction in the non-tubercular

the reason being that the healthy body may occasionally contain sufficient tubercular lysin to react to Tuberculin. It must be realised that Lysin is present in everyone. Were it not so the body could not be harmed by Tubercular infection. In fact Ehrlich's theory depends on anti bodies, including lysin, being present in small quantities in the normal body. They are merely increased by the action of antigen. On the other hand, reactions are sometimes absent in the undoubtedly tubercular.

A. In slight cases in the quiescent stage, the explanation being that the lysin action is reduced to a minimum by the subsidence of the tuberculous process. Consequently, the small amount of Tuberculin injected does not furnish enough lysinized Tuberculin to produce a reaction.

B. In severe cases of tuberculosis there are three explanations of this.

1. The body containing excess of lysinized Tuberculin the extra Tuberculin injected has no effect.

2. The tissues are too damaged to manufacture lysin.

3. The lysin has been neutralized by the tuberculosis and there is no free lysin for the Tuberculin to act upon.

The Lysin Theory explains why you get a reaction in apparently cured tuberculosis. These individuals may have sufficient lysin in the body to produce a reaction. Negele and Burckhardt have proved that there are inactive foci in

nearly every adult and therefore the value of the Tuberculin reaction for diagnostic purposes is much lessened. Von Pirquet's reaction, for this reason, has fallen into disrepute. It is too delicate.

Sahli gets over this to some extent. He uses dilutions 1 in 10 ; 1 in 100 ; 1 in 1,000, of old Tuberculin. If they react to 1 in 10 then he passes on to 1 in 100, and so on until a negative result is obtained. It shows the capacity for reaction, though possibly not the degree of activity. We use dilutions 1 in 10 ; 1 in 100 ; 1 in 500, as a matter of routine at Margaret Street Hospital for Consumption, and these, if taken in conjunction with clinical and X ray examinations, have proved of real value. A reaction of 1 in 10 is of little diagnostic value, but greater dilutions, such as 1 in 100, or 1 in 500, if at all marked, are an indication to go very cautiously with Tuberculin treatment. Sahli considers that you should be able to get an idea of the initial Tuberculin dose by this method and I make use of it myself at Margaret Street. If I get a reaction with 1 in 500 I prefer not to treat at all, or at any rate to begin with very minute doses. 1 in 100 demands caution, but 1 in 10 (comparatively non-sensitive cases) you can begin with, say, .0001 cc of T.A.F. Sahli is against subcutaneous injections for diagnostic purposes as he considers them to be dangerous. His reason for this opinion is that it is dangerous to overload a patient

with a toxin merely for purposes of diagnosis. He points out, however, that the slight reactions which are produced with small doses of Tuberculin in doubtful cases are often of great confirmatory value.

I think in this statement Sahli errs on the side of caution. I admit that it is inadvisable to give test doses in obvious cases of tuberculosis and agree with him that they may do harm, but in the border-land cases, without tubercle bacilli in the sputum, and without definite clinical manifestations, and without fever, I have never seen any harm result in test doses. In fact in many cases there is a marked improvement in weight and general condition, and in these cases it is obviously unnecessary to go on to higher doses merely for diagnostic purposes. I am thoroughly in accordance with what he says of the diagnostic value of slight reactions with small doses in treatment.

Sahli points out that there is a very close connection between hyper-sensitiveness to Tuberculin and immunity to tuberculosis. According to Wolff-Eisner's theory hyper-sensitiveness is due to lysin which, as has been shown, is increased in the tubercular. Hamberger concludes that this hyper-sensitiveness is an effort of the organism to repel the infection, which implies a certain degree of immunity against tuberculosis.

That this is true I have no doubt whatever, one sees it every day in the practice of Tuberculin. The hyper-sensitive

cases are by no means the most unfavourable cases as far as prognosis is concerned, and the opposite, vis; the sub-sensitive, do not always in the long run do so well as those first named.

Bail brings to notice the unfavcurable side of hyper-sensitiveness. He proved that if large doses of tubercle bacilli are injected into tubercular guinea-pigs they die in a few hours, whilst normal guinea-pigs similarly treated, only show symptoms after 24 hours, and this, taken with the fact that small doses of Tuberculin which are quite innocuous to a healthy guinea-pig will kill a tubercular guinea-pig.

Hyper-sensitiveness is due to the fact that the tubercle bacilli and the Tuberculin have been converted into a dangerous toxin by the presence of the increased amount of lysin caused by the injection.

If small quantities of Tuberculin are used lysinized tuberculin is formed, and acute inflammation is the result. This does not develop because these reactions are protective and also because not only is the Tuberculin lysinized, but also probably the living tubercle bacilli which are killed as the result of this action.

On the other hand, if too large doses of Tuberculin are used the amount of lysinized toxin may be sufficient to destroy the animal. Thus, Tuberculin, when used in the hyper-sensitive is a double-edged tool. It may do much good, as

one often sees a gain in weight, increase of appetite, and so on. On the other hand, you too often have the reverse side of the picture. Certainly any man who has experience of Tuberculin, whether he believes in the Lysin Theory or not, proceeds cautiously, or not at all, with hyper-sensitive cases.

Romer, experimenting on cattle immunized against human tubercle bacilli and untreated cattle, found that the latter died when injected with a large dose of tubercle bacilli, although they showed no attempt at reaction. The former, however, had severe reactions, but recovered. This proved that immunity and hyper-sensitiveness go hand in hand.

Sahli considers that the immunity which is produced by Tuberculin is not because the patient becomes immune to intoxication by insensitiveness to the poison, but rather just the opposite, viz: a hyper-sensitiveness in which the body, as it were, nips the infective agent in the bud. In this case there may be no clinical manifestation of hyper-sensitiveness. We must suppose that the hyper-sensitiveness has so perfectly stimulated the protective cells of fluids that the toxin is powerless to cause a reaction. In a similar manner Tuberculin in the right doses may produce no reaction, the lytic action being at once counteracted by the anti toxic action established. Sahli considers that this same hyper-sensitiveness explains recurrent attacks of acute rheumatism

pneumonia, and erysipelas. As a result of a former invasion and redovery hyper-sensitiveness is acquired and so relapses occur frequently, but owing to the establishment of specific anti bodies recovery is quicker than in a primary attack.

The experiments in super injection explain why, although tubercle bacilli are in the blood stream, the disease seldom attacks fresh organs, the reason being that hyper-sensitiveness has been established and the disseminated tubercle bacilli has been rendered harmless by the lysin. It also explains the comparative rarity of laryngeal tuberculosis in open tuberculosis of the lung; were it not so, the larynx would almost bound to be infected by the tubercle bacilli during expectoration.

The theory of protective hyper-sensitiveness is well borne out by the fact that children who have recovered from tuberculous adenitis seem less prone to serious tubercular lung affections. This hypothesis also goes far to explain immunity to the disease. People from comparatively tubercular immune areas, such as we may suppose the Highlands to be, if they migrate, say, to Edinburgh where the disease is prevalent, contract the infection in an acute form. The reverse applies in towns where the disease is prevalent. Morbidity is high, mortality low. This may go a long way to explain the lessened mortality from tuberculosis at the present time. An analogy is found in the incidence of typhoid fever in India, at one time it was supposed that the native of India was immune. It is now

known that this is not the case, He has probably established a hyper-sensitivity by constant exposure to infection.

The almost universal hyper-sensitivity to Tuberculin is proved by Von Pirquet's test which is nearly always positive in adults. Hence Wolff-Eisner concludes, with justice, that as inactive tuberculosis which is present in most adults is protective against any but the severest forms of the disease, it is really only necessary to protect against massed infection.

Wolff-Eisner explains fever, and falls of temperature, and night sweats, as due to tuberculosis resulting from hyper-sensitiveness. He considers that it is due to lytic action on the products of the tubercle bacilli becoming absorbed in the blood stream. He also considers that rises of temperature as the result of exercise in the tubercular are due to the fact that on account of this more blood is brought to the tubercular focus and as a result, more tuberculin is absorbed and lysinized in the blood stream. Sahli states that absorbtion of bacillary protein in small doses causes a rise of temperature, and in large doses a fall.

All this is most important. If one studies Patterson's Charts, in which the result of exercise on the temperature is recorded, one is struck with the similarity they have to Tuberculin temperature charts. In both series, in most cases, benefit is observed by graduated treatment, and in both series also the harm of Tuberculin or exercise in unsuitable cases is

obvious. One is also able to understand why Tuberculin should be avoided, or used with the greatest caution, in febrile cases.

Sahli then goes on to discuss the general surgical treatment of Tuberculosis, and Tuberculin treatment, in the light of the Lysin Theory, and below will be found a brief summary of his views.

He explains the benefit of removal of large tubercular foci on the remaining foci as follows: By the removal of the large focus, which absorbed lytic and anti toxic anti bodies, a large amount of these are left free in the blood stream and so are able to deal with the smaller foci. Moreover, an excess of toxin is removed by extirpation of the diseased focus with general benefit to the patient. Bahrot found that in tubercular guinea-pigs if part of the diseased tissues be removed they become less sensitive to Tuberculin, and the animals are less easily killed by Tuberculin injections. He explains further, why in some cases extirpation of lymphatic glands results in improvement and sometimes in dissemination of the disease. It depends upon the degree of lytic/action and hyper-sensitiveness of the organism. In the first case this is sufficient. In the second case, the disease being inactive, the lytic action is insufficient to resist the spread of the bacilli.

He considers, therefore, that a cutaneous test should be performed previous to operation.

He believes that there is a true immunizing action established as a result of Tuberculin therapy and that this is not due to Tuberculin, but due to Tuberculin lysin. He considers that Wright's experiments with opsonins point to the existence of anti toxins in tuberculosis. He points out that in all endo-toxic affections it is probable that the anti toxic substances probably remain localized in the foci and do not get into the blood stream - hence they cannot be isolated, and so the presence of these anti bodies, though they almost certainky exist, is difficult of proof. One significant fact is that increasing doses of Tuberculin diminish sensitivity. This must be due to an anti toxin. Were it not so each dose of Tuberculin would tend to increase the hyper-sensitiveness. He defines the action of Tuberculin treatment as follows:

By progressive doses the lysin is increased. In consequence bacteriolysis takes place and the lysinized Tuberculin sets up an irritative immunizing action in the foci. The acute toxic action is, however, increased in a higher proportion: hence reactions can be avoided by careful dosage.

The Lysin Theory explains why highly sensitive cases often do extremely well under Tuberculin. Sahli suggests that these cases might be diagnosed by a modified cutaneous test. This

we now employ at Margaret Street Hospital, as before stated, and treatment modified accordingly.

Sahli states that no complete immunity to tuberculosis can be obtained by previous tubercular treatment. For this reason it is impossible to protect the still healthy individual. Von Behring has, however, immunized cattle against bovine tuberculosis by means of attenuated human tubercle bacilli.

Nathan Raw (B.M.J. April 1921) has attempted to immunize human beings with attenuated bovine ~~cultures~~ Cultures, his view being that bovine and human bacilli are antagonistic to each other.

Assuming that the common feature of living tubercle bacilli and Tuberculin to be hyper-sensitiveness, the difference in the two appears to be one of degree, the former causing greater hyper-sensitiveness. So, provided correct doses of Tuberculin be given, rising so as to correspond as far as possible with what may be supposed to occur in progressive disease, there are no signs of reaction. Moreover, the chemical action of tubercle bacilli and Tuberculin is, as has been proved, identical, as anatomical tubercles can be produced by Tuberculin.

The reason why reactions occur at the beginning of treatment and tend to subside, or not occur at all, is probably because though the Tuberculin is lysinized in increasing quantities it is neutralized by the anti toxins of the body, so that

hyper-sensitiveness is marked. This marked hyper-sensitiveness is an obstacle as the most important point in immunization is hyper-sensitiveness with its inflammatory and bacteriolytic anti actions. But this obstacle, viz: toximmunity to lysinized Tuberculin is what is aimed at by the reactionless method. In contrast to Koch's original treatment with living tubercle bacilli where there is no such toximmunity. That this is so is proved by the fact that in infected and super-infected guinea-pigs an inflammatory reaction is instantly produced as a result of super infection. Again, in cattle immunized by living bacilli, the absence of toximmunity is shewn by the fact that though they resisted the first infection successfully, the second infection produced an acute inflammatory reaction.

The difference between the action of living bacilli and Tuberculin appears to be that in the former the Tuberculin actions are gradual, in the latter sudden. A second explanation is that "the production of the substance causing the protective hyper-sensitiveness to living bacilli - the lysin - is not sufficiently stimulated by the Tuberculin as such, but that the lysin is chiefly or entirely elaborated in the anatomical foci from the tissue cells under the influence of the Tuberculin which is contained both in the tubercle bacilli in the foci and in the circulating blood. Thus the formation of lysin chiefly takes place in an organism with tubercular changes and not in the healthy body."

From these two explanations Sahli concludes that Tuberculin is a real tubercle toxin.

Sahli is impressed with the importance of hyper-sensitiveness and considers that this should be our aim by some modification of technique, but at present frequent doses and massive single doses seem to have failed to produce this.

It seems to be clear that Tuberculin is not specific and that there is no antidote other than tubercle toxin, which stimulates two sets of anti bodies, the "primary" which weaken the tubercle bacilli and cause general and local reactions, and the "secondary" which act against the lysinized Tuberculin and lysinized tubercle bacilli. Under this reasoning the necessity of small and gradually increasing doses becomes clear, The aim should be the stimulation of the natural healing forces, following the means followed in spontaneous case, viz: the production of tox-immunity and the stimulation of the local healing forces in the tubercular foci. In other words, it is a relative immunity which is our goal and is aimed at by stimulating the body cells. In short, one cannot help coming back to the original idea. There are no specifics. All we can do is to assist nature. If one grips this idea one can do much good with Tuberculin; if one fail to see it, untold harm.

PERSONAL CLINICAL EXPERIENCE IN THE USE OF TUBERCULIN.

Introductory.

Perhaps I may be permitted to give a few words of explanation as to why I took up Tuberculin at all, as it has some bearing on the line of treatment I have followed.

In 1920 I had the good fortune to be appointed assistant physician to Margaret Street Hospital for Consumption and Diseases of the Chest, and about the same time became clinical assistant to Dr Henry Campbell at the West End Hospital for Diseases of the Nervous System. When Dr. Campbell heard that I was interested in tuberculosis he kindly gave me an introduction to Dr Camac Wilkinson, who was at that time in charge of a Tuberculin dispensary in Chelsea. Dr. Wilkinson was extremely courteous to me and gave me permission to attend his clinic whenever I felt inclined. I took full advantage of his permission and attended there regularly every Thursday for eighteen months. I had no knowledge from a practical point of Tuberculin and went there with an open mind as to

its value or otherwise.

It took me a long time to understand what it was all about, but gradually it dawned upon me that the people under this treatment, without any medicine whatever, were improving steadily, whereas a similar type of case whom we were dealing with at Margaret Street with drugs, without Tuberculin, were certainly not improving to a similar extent. This induced me to study the matter further. I mastered Wilkinson's book, and later on read other works on the subject. By the kindness of Dr. Wilkinson I was permitted to treat a case from start to finish, he prescribing the doses for me. He considers that no man should attempt to treat tuberculosis with Tuberculin unless he has watched a case through a course from start to finish under an expert, and has carefully studied 100 charts and case sheets. This involves a study of at least six months duration and I am convinced that it is none too little.

I gradually then, as opportunity arose, began to use Tuberculin in private practise for diagnostic purposes and if I got a reaction I treated them with Tuberculin. As time went on I used it more and more extensively. By the courtesy of Dr. Henry Campbell I have a clinic at the West End Hospital for nervous diseases. I work there at cases diagnosed neurasthenia and very carefully check these, and a proportion of those in whom I suspect tuberculosis as being the cause of the neurasthenia, I test and treat with Tuberculin.

Six months ago I established a Tuberculin clinic at Margaret Street Hospital and, through the kindness of the staff, I have been able to deal with a fair number of cases. From these various sources then I have been able to collect the cases recorded in this thesis, and have come to certain conclusions which I shall hereafter relate, as to the value of Tuberculin in the treatment of tuberculosis, and the position it should hold in Tuberculin therapy.

My Method of Using Tuberculin.

I realize the primary importance of clinical methods and use Tuberculin rather as a confirmatory test than as a means of diagnosis. I make especial note of the symptoms, invariably take the blood pressure, when feasible have a skiagram taken of the lungs, and in certain cases when it is deemed desirable I have an examination made of the urine, which sometimes affords very valuable information as to metabolic changes. In addition to this I make a rough estimation of the haemoglobin and calcium content of the blood.

Of the signs one need say little; I simply follow orthodox methods, but to detect early tubercle of the lung by means of physical signs alone is not possible. Positive signs are of value, negative of comparatively little use unless confirmed

by other methods (such as skiagraphy). Symptoms in early tuberculosis are of more value than signs. It is not my purpose to discuss these in this theses beyond pointing out that generally speaking they are those of a toxaemia.

With regard to blood pressure, other things being equal, a low blood pressure is usually present in tuberculosis. High blood pressure, of course, does not exclude this disease, but it is not nearly so common as the opposite.

A skiagram is an immense help. It gives one a very good idea as to the presence or absence of activity, and it is extraordinary how closely it coincides with the diagnosis made by the multiple cutaneous reaction. The readings should always be made by an expert.

With regard to the metabolic changes in the urine I prefer to say little, as the problem is being worked out by Drs. Campbell, McClure, and Ellis, of Margaret Street Hospital, and the matter is still sub judice.. But there appears to be a tendency to alkalinity in cases of tuberculosis, speaking generally.

Testing the coagulability of the blood is useful. It may indicate ~~points to~~ Calcium deficiency, which is usually one of the signs of tuberculosis.

I need hardly mention that an examination of the sputum for tubercle bacilli does away with further diagnostic methods, but it is, of course, desirable to make a diagnosis before the

case has advanced as far as this, for it is in the early cases that the best results are obtained with Tuberculin.

Having then established a great possibility of the case being tubercular, I proceed to test them with Tuberculin.

I am fully aware of the fallacies of the Tuberculin test. The frequency of cases which react to it, the doubts which have been thrown as to whether it denotes activity, or simply latent tuberculosis, and so on. Again, there is the question of its safety or otherwise to be borne in mind. With regard to the latter point, it seems to me to entirely depend on the class of case in which you use it. Luckily, in the obvious cases there is no necessity to employ it. In the doubtful cases, when it is of such value, I have never seen any harm done. In fact quite frequently there is an increase in appetite and body weight, and a diminution of symptoms. This is in itself a diagnostic point. Sahli, who is against diagnostic injections, acknowledges that such changes after therapeutic doses help to confirm the diagnosis, for the effect of these doses on the non-tubercular is practically nil.

The fact that so many react to Tuberculin does not seem to me to be an argument against its use. No one nowadays, would I imagine, test the healthy with Tuberculin. It is only when a person goes sick with symptoms pointing to an upset of the "Tuberculin Balance", if one may be permitted to coin an

expression, that one tests them. If you do not test your cases and are a believer in therapeutic doses, as Sahli is, I fail to see how you can avoid sometimes putting a patient through a long course of treatment who is really not tubercular at all. I know I should have done so had I not employed the diagnostic test. As to whether the test demotes activity or not is a very difficult question indeed, but the fact that symptoms clear up remarkably sometimes under treatment does point to there being some active lesion somewhere, perhaps too small to be diagnosed by clinical methods.

The multiple cutaneous Tuberculin test, which I have dealt with elsewhere, appears to coincide very closely with the physical signs of the skiagrams. In fact at Margaret Street Hospital a diagnosis is made on the sum total of the three sets of phenomena, viz: physical signs; X ray appearances; and the multiple cutaneous reaction. Positive physical signs outweigh the other two, but in the absence of these the latter are of great value.

In my own practice I employ the intra muscular diagnostic test, which I learnt from Camac Wilkinson. I do so because, I think, it requires great experience to be able to form a correct interpretation of the cutaneous reaction, valuable as it is in certain hands. I also find that the intra muscular method in my hands has two advantages: 1. It is not too delicate. 2. You can get a rough idea as to what initial

treatment dose you can commence with to best advantage. At one time I used this test more or less as a routine, but since reading Sahli's work I confine testing to cases in which the diagnosis is doubtful. In most cases I begin testing with a lower dose than that advocated by Camac Wilkinson, nor does it appear necessary, or desirable, to have a severe general, focal, and local disturbance. Cochrane and Sprawson (Guide to the Use of Tuberculin) object to diagnostic injections on the ground that by so doing you may produce hypersensitiveness, and this is undoubtedly (though not, I think, usually) the case.

On no account should this diagnostic test be applied ~~[illegible]~~ in febrile cases. On that point all authorities are now agreed.

Having decided to give a diagnostic injection, I present the patient with a chart (Fig 1) and instruct him to take his temperature in the mouth for five minutes 4 times daily, and record it on the chart, and to have his weight taken. Similar charts are used throughout treatment and the weight is recorded once a week. In hospital treatment I record the weight bi-weekly. Cochrane and Sprawson advise a daily record of weight, but, except in an institution this is hardly practicable for most cases. I find that the simpler and less irksome you make the routine the more readily patients obey your orders.

FIG. 1.

REPORT.

Name..... *For Week Ending*.....

	TEMPERATURES.				HEALTH REMARKS.
	8 a.m.	12 noon	4 p.m.	8 p.m.	
SUNDAY					
MONDAY					
TUESDAY					
WEDNESDAY ...					
THURSDAY					
FRIDAY					
SATURDAY					

Weight.....

For diagnostic purposes most people use Old Tuberculin, I prefer T. A. F. (Tuberculin Albumose Frei) because, being free of albumose. it is not so delicate in its action. Another reason is that it seems to be advisable to test a person against the tuberculin with which you are going to treat that patient, therefore, as I invariably now treat patients with T. A. F., I prefer to use that Tuberculin in diagnosis. The initial dose I begin with for diagnostic purposes is T.A.F. ·0005, or under. If no reaction is observed I give ·001, then ·002, ·004, then ·01. If there is any sign of a reaction I either consider the diagnostic dose has been given or repeat the dose.

I classify my cases into hyper-sensitive, - those reacting to 00005 and under, normal sensitive, - 001 to 002, subsensitive, - ·003 and over. The classification is a rough one, but helps one in deciding on the initial treatment dose, a point of great importance. I will, however, deal with this matter when I come to treatment.

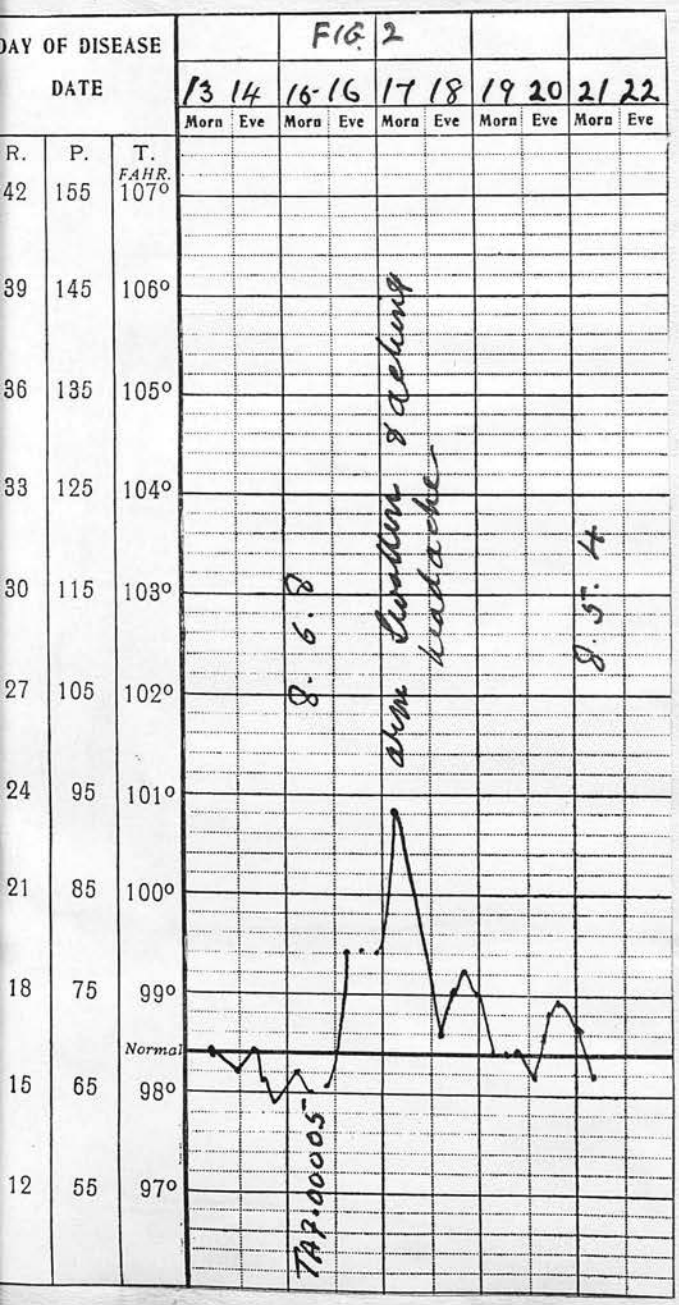


FIG. 2.

Hypersensitive.
Severe general and local reaction, lost one pound in weight.
Soon lost sensitiveness under subsequent treatment and gained 8 lbs.

During diagnosis I warn people that they must expect some reaction and that if it occurs they should rest and bathe the arm with hot water. I find that, probably as the result of education in the effects of enteric innoculation during the war, a reaction does not, as a rule, alarm the patient.

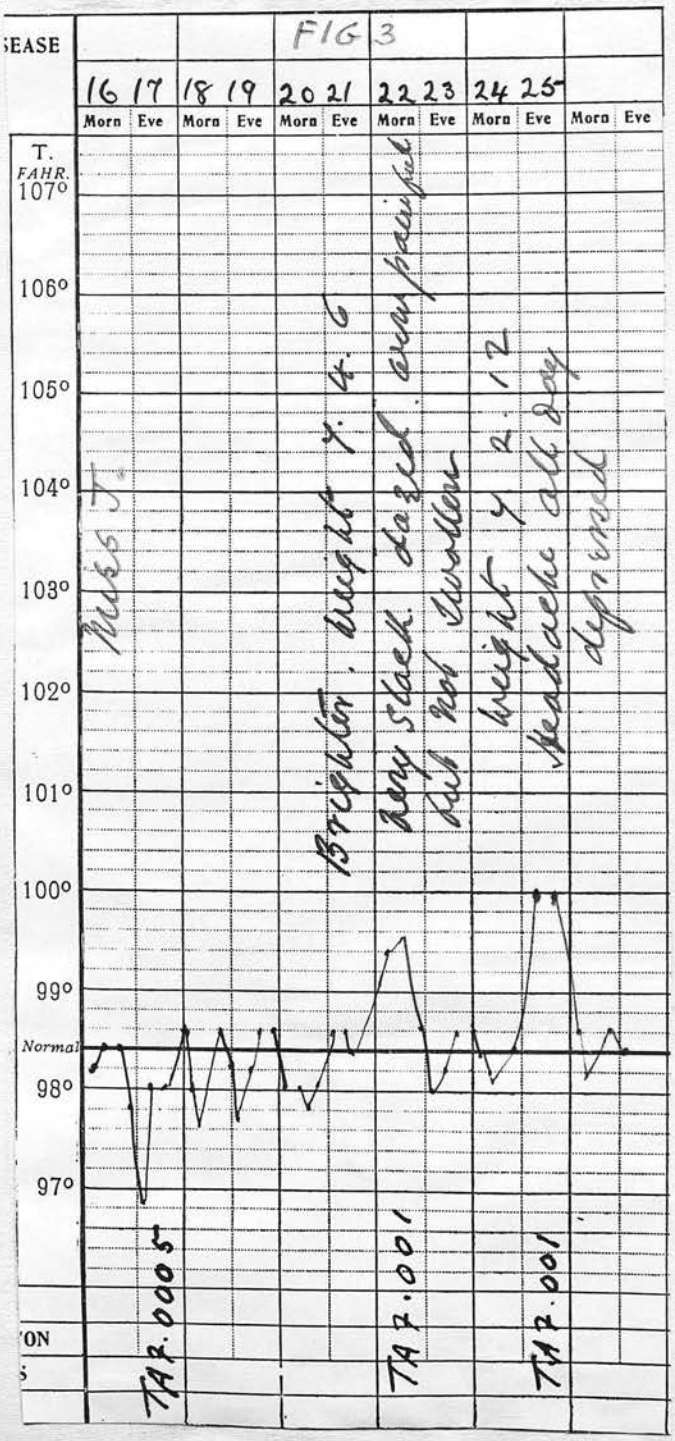


FIG. 3.

Normal Sensitive.

No reaction with .0005.

Some reaction with T.A.F. ·001, and on repeating dose, greater reaction. Lost nearly 2 lbs.

With my present knowledge I should not give the second dose of .001 in a case of this type.

Did well under treatment, gained 5 lbs.

Figs. 2, 3, 4, and 5, show specimens of reactions according to classification. Fig. 6., shows a negative result. I have seldom seen any ill effects from these test doses, in fact they often seem to do good.

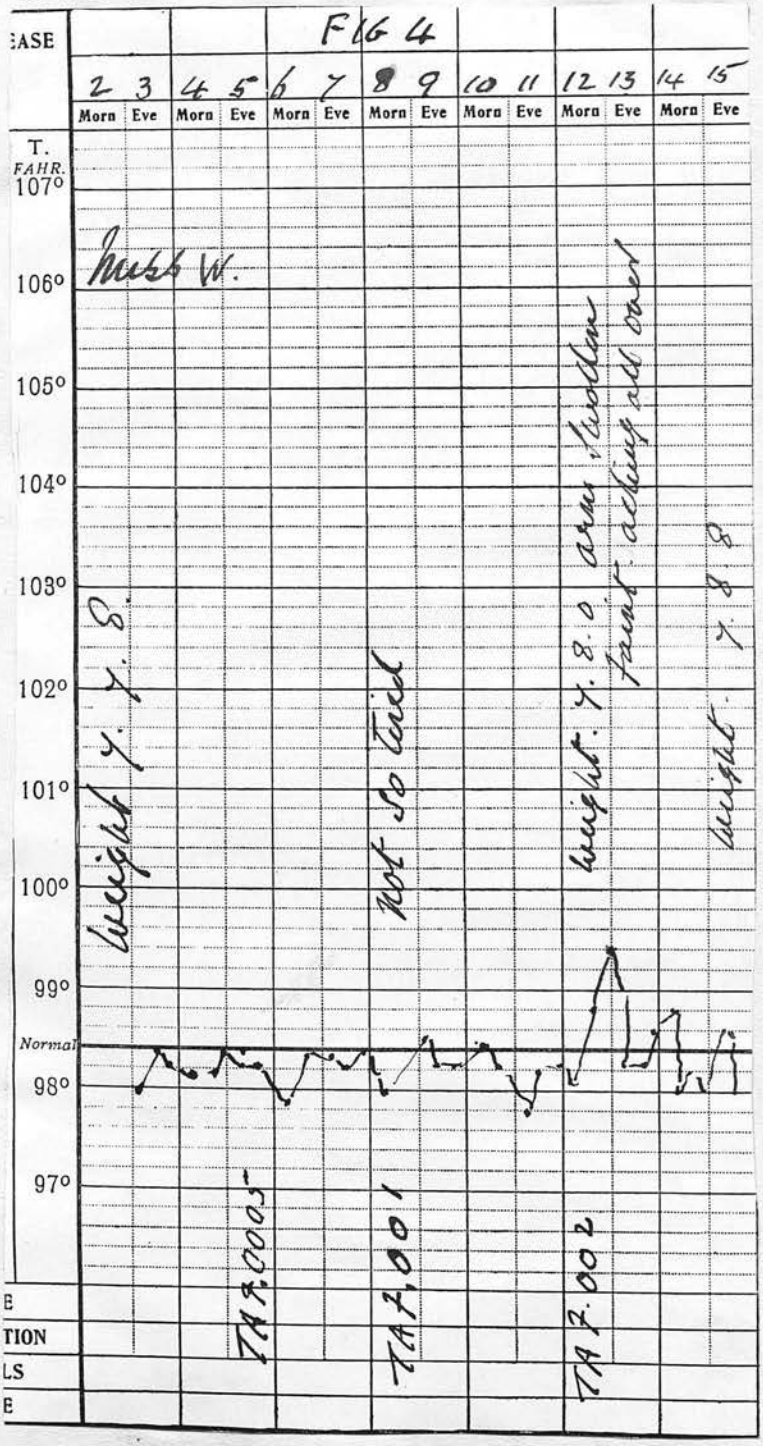


FIG. 4.

Normal Sensitive. No reaction with 0005, or .001. Reacted to .002. Had the dose been repeated it is probably that the reaction would have been excessive.

In patients who are neurasthenic you should proceed with caution and be content with some indefinite symptoms, such as headache and slight local reaction. If you push your dosage too much you are apt to frighten your patient, and as a result they may refuse to go on with the treatment.

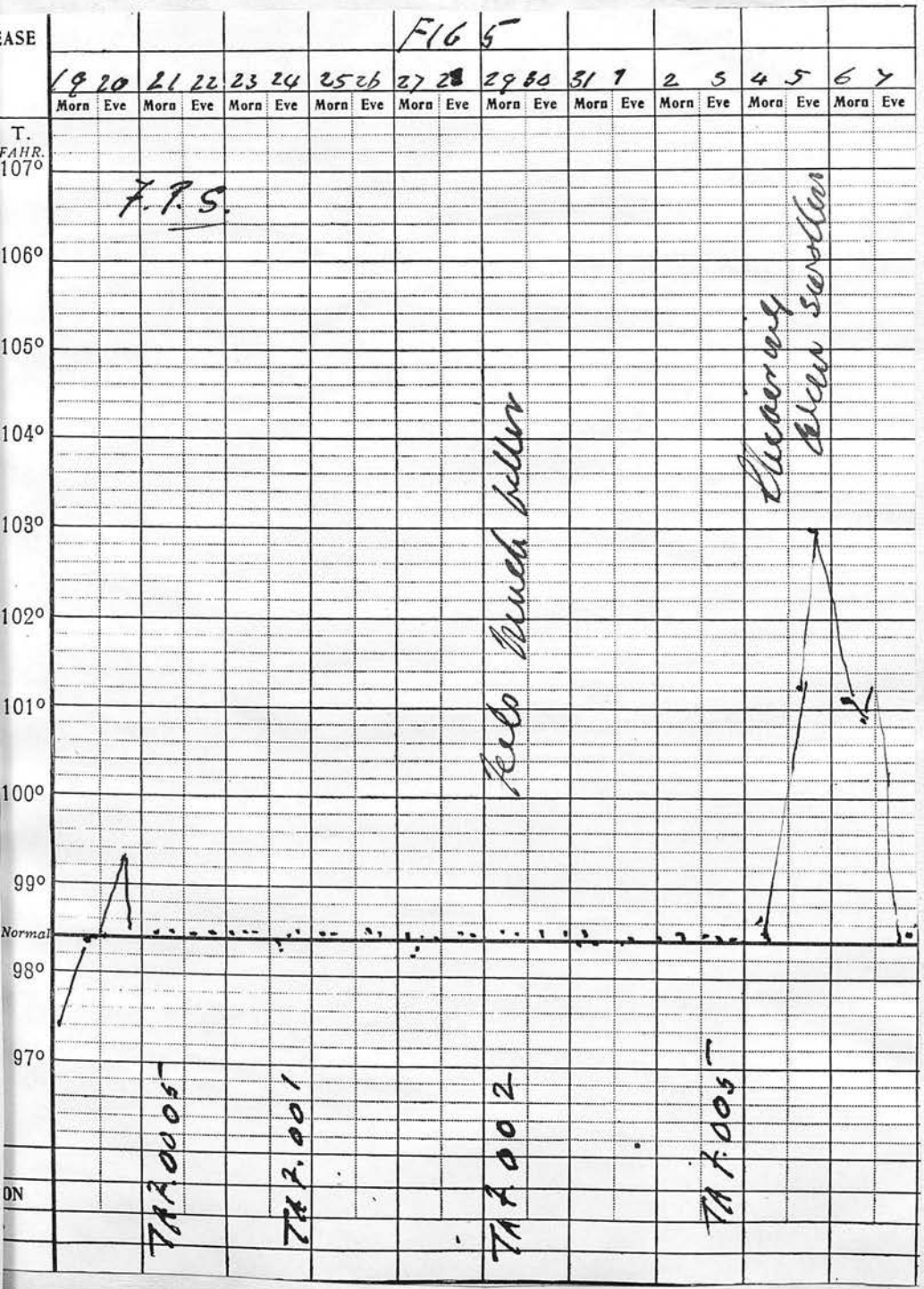


FIG. 5.

Subsensitive Case. No reaction till T.A.F. .005 had been reached. Note very even temperatures. Completed course with no further reactions. Gained 8 lbs.

In fact, in all cases, I now go cautiously with testing. As one's experience increases one realises that the majority of people, even those in what is commonly called good health, will react to Tuberculin if a sufficient dose is given.

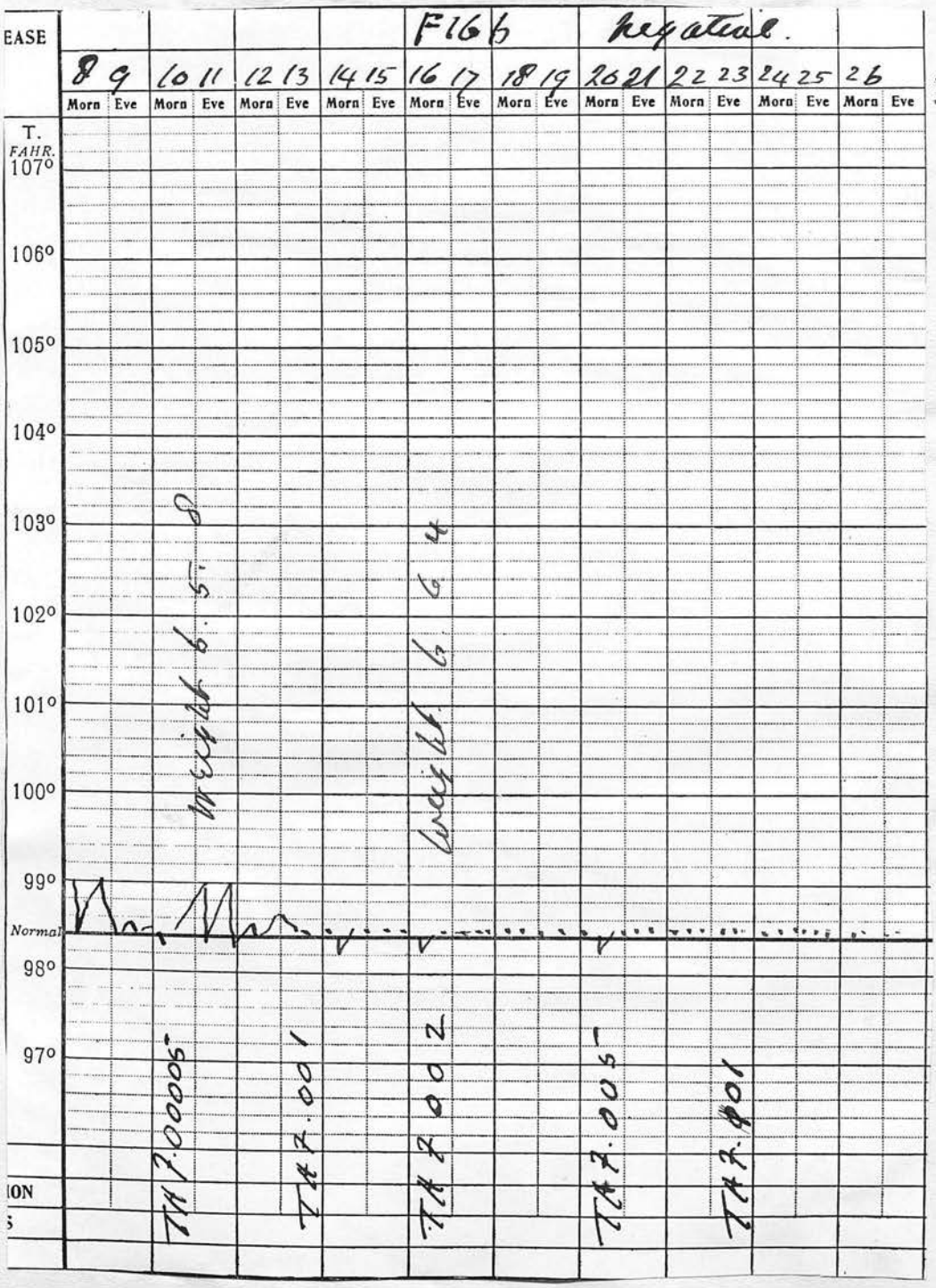


FIG. 6.

No attempt at a reaction. Note the very even temperature throughout period of testing.

One also realises that severe cases may not react at all, and that hyper-sensitiveness points to by no means an unfavourable prognosis. At the same time it is too good a thing to discontinue for theoretical reasons. There is one matter in which it is of the greatest assistance, and that is the initial treatment dose. Till someone can definitely state from the multiple cutaneous reaction what the initial treatment dose should be, it seems to me that intra muscular diagnostic injections must be employed. I am gradually coming to some conclusions on this matter, viz: the value of the multiple cutaneous reaction from this viewpoint, but my observations are at present insufficient.

Granting that Tuberculin is of service in many cases, and granting that it is of disservice in others, which most people allow, and granting that there does not seem to be very much to choose between the various preparations, the question must resolve itself into one of dosage. It appears to me that the only rational way to get to this at present is to give test doses, and when you get a reaction to wait awhile and begin again with a smaller dose of the same Tuberculin given in the same way. If this causes a reaction wait again, and try again with again a smaller dose. Wilkinson considers that it is the large doses which do good, and I gather from watching him that he begins his initial treatment dose, when he can,

with T.A.F., '0001, but that in a hyper-sensitive case he drops much lower than this, but with regret.

Wright, and Professor Eyres of Guy's, belong to the small dose school, but I understand they deal chiefly with surgical tuberculosis, which cases tend to be hyper-sensitive.

Speaking in the most general terms, I should say, from a bird's-eye view of the problem, that in severe cases of tuberculosis without mixed infections, you can push Tuberculin without any effect. The patient is already manufacturing so much that the little more you put in has little effect for good or ill. That they die is no proof; they will die in any case. But in the hyper-sensitive you may kill that hyper-sensitive resisting power, and may do an infinity of harm. The art seems to be to overcome that irritability without harm, and it is in these cases that my chief interest lies. I realise that health matters, not life, and appreciate Sir Andrew Clarke's saying:- "Return to the ways of physiological righteousness." I also believe that the same results can be obtained by sanatorium treatment on the lines of Patterson of Frimley. He apparently manufactures Tuberculin by natural means, viz: by graduated exercises.

The chief role of Tuberculin, I am convinced, is in ambulant cases, and though I readily concede the value of

Sanatoria, a method which can be pursued without the expense of sanatorium treatment, such as the reactionless method of Sahli, must receive serious consideration. Whether it is specific, or simply imitates nature's method by increasing the resisting power of the body cells, is a difficult matter on which to form an opinion. That it does good when properly used, there is little doubt.

Technique.

This seems to be a suitable opportunity for describing the technique I use, before entering upon the details of treatment. A technique, to be satisfactory, must be simple, and must be reduced as nearly as possible to a matter of routine.

My impedimenta are: 1. A small sterilizer. 2. A glass syringe of about 1 cc content, and No. 17 record needles. 3. A 1 .cc glass pipette graduated in $\frac{1}{10}$ ths of a.c.c. 4. A $\frac{1}{10}$ of a.c.c pipette graduated in $\frac{1}{100}$ ths 5. Methylated spirit to clean the pipettes. 6. Normal saline solution. 7. T.A.F. Tuberculin albumose free. 8. A spirit lamp.

I have had made for me a stand to hold the pipettes; see accompanying sketch. (last page)

It is so arranged that I can swing the pipettes to any angle without removing them from the stand, a matter of

considerable importance in practical working.

I make up my dilutions as follows;

From the original solution, which is in a 1.c.c. bottle, I make a 1 in 10 solution by taking . 9.c.c. (using the large pipette) of salt solution, and . 1.c.c. (using the small pipette) and mixing them in an empty 1.c.c. bottle. To make a 1 in 10 dilution a similar proceedure is adopted, but substituting 1 in 10 solution for the original. In a similar way 1 in 1000 and so on are prepared.

In this way I have a series of dilutions arranged in serial order and kept in a special stand which can be depicted diagrammatically thus:

1 in 100,00	1 in 10,000	1 in 1,000	1 in 100	1 in 10
1	2	3	4	5

Original
6

Suppose I wish to give . 0000001.cc T.A.F. I remove the plunger of the syringe, fill the 1 cc pipette up to a convenient extent, say, .75 of a c.c. with the salt solution diluent. Then into the smaller $\frac{1}{10}$ of a c.c. I fill up to the bottom mark, which has a capacity of .01 of a c.c. with 1 in 100,000 solution. I then eject the salt solution into the barrel of the syringe, then into the barrel I insert the smaller pipette and mix the solution well by shaking up and expelling. The remainder of the process consists in giving

the injection into the patient's arm in the usual manner. The belly of the triceps is a convenient spot and the injection should be given, if you use a fine needle such as I suggest, with the patient's arm relaxed as otherwise you are apt to break your needle.

Exactly the same proceedure is followed with the higher doses, except that when I get to .1 of the original solution I do my measurements with the 1.c.c. pipette reserving the small pipette for the diluent. If you use the small pipette for big doses you have to fill it several times and can easily miscount. Besides, it takes longer. I need hardly say strict asepsis is observed.

Treatment.

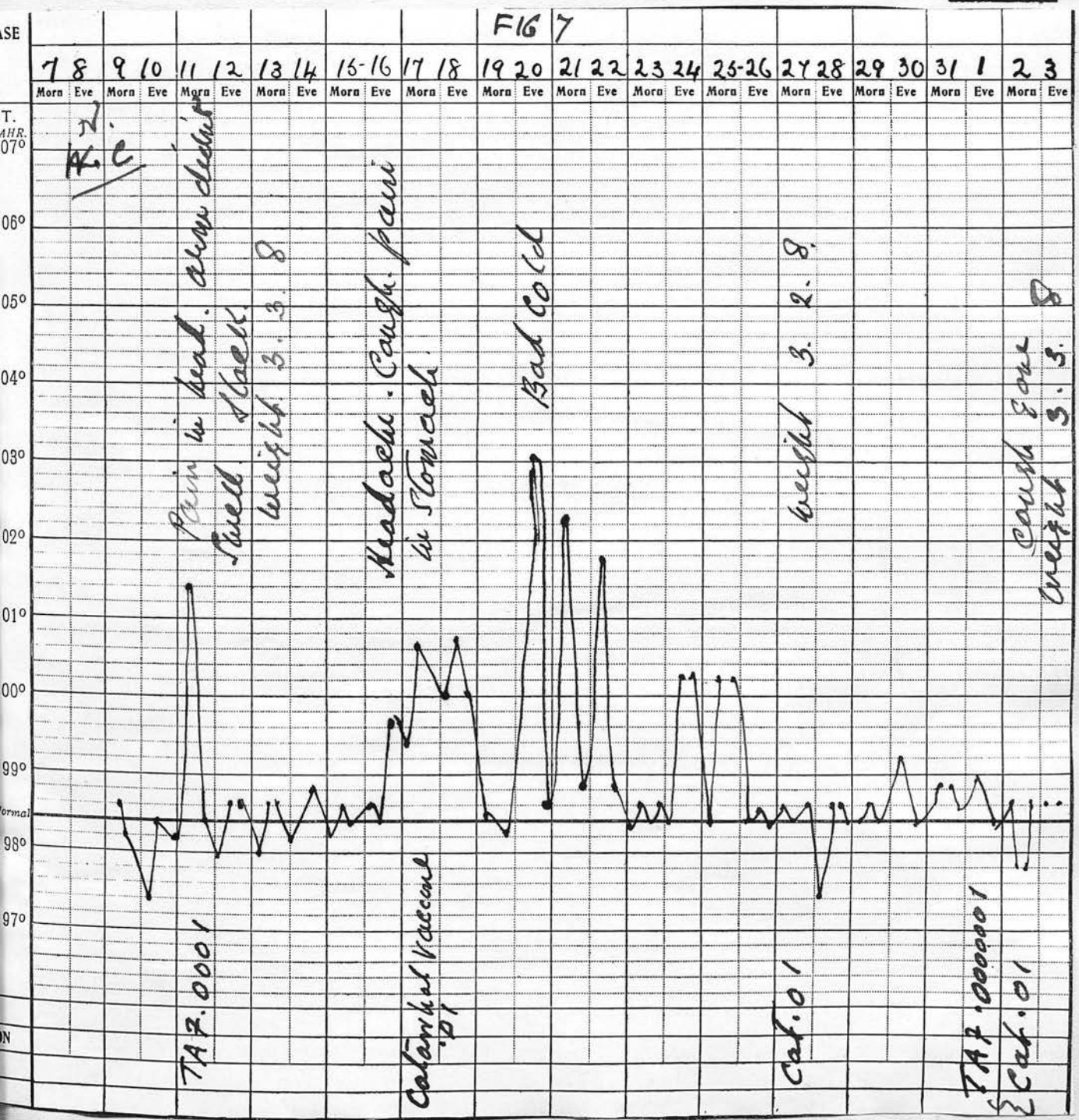
This may all be summed up in one word and that is"dosage." Everything depends on this, and dosage depends on one thing, and that is sensitiveness. It is really out of the hands of the physician. It is decided by the patient and the Tuberculin. I am, of course, pre-supposing that you belong to a school who prefers to proceed without reactions, or at any rate slight ones.

My experience is the same as Camac Wilkinsons, that it is the big doses that really do good and, therefore, one should presumably begin with as large doses as one can without doing harm. There is no royal road to fixing the initial dose, but

one gets a fairly good idea from the diagnostic reaction.

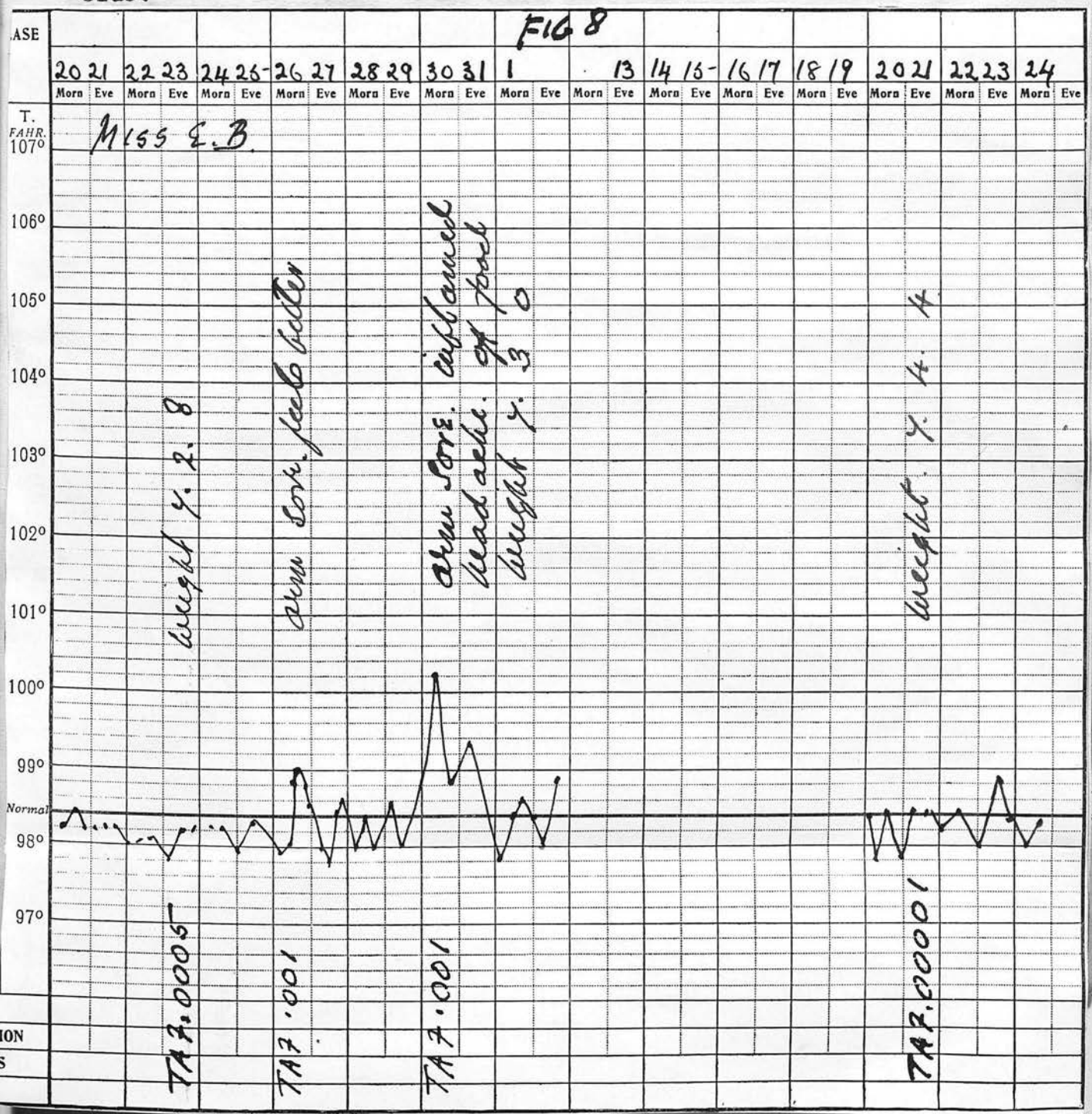
For instance, Boy. N.C. Fig. 7. reacted severely with T.A.F. 0001.

FIG. 7.



It would have been obviously unsound to attempt further dosing for some time, so I treated his cold with a detoxicated coryza vaccine, and later combined this catarrhal vaccine with a small dose of T.A.F. which he stood quite well. I may say that if I get a reaction with .0005 or under I always reduce the irritant treatment dose to .0000001. It may not be absolutely necessary in all cases, but I prefer to be on the safe side.

FIG 8



Contrast the last case with that of Miss E.B. Fig. 8.

There was a slight reaction with T.A.F. .001. It would have been wiser perhaps to have been contented with that reaction, but I wanted to confirm it, so repeated the dose with the result that the disturbance was somewhat severe. Owing to a holiday there was a longish interval before the initial treatment dose of T.A.F. 0001, which caused no reaction. There were no subsequent reactions of importance during treatment.

Fig. 9. is an example of a case which reacted to .002 without a severe reaction. Next time I gave an initial treatment dose of .0001 and doubled up rapidly till T.A.F. .001. After this I went more slowly, but she completed the course without further reactions.

FIG.9.

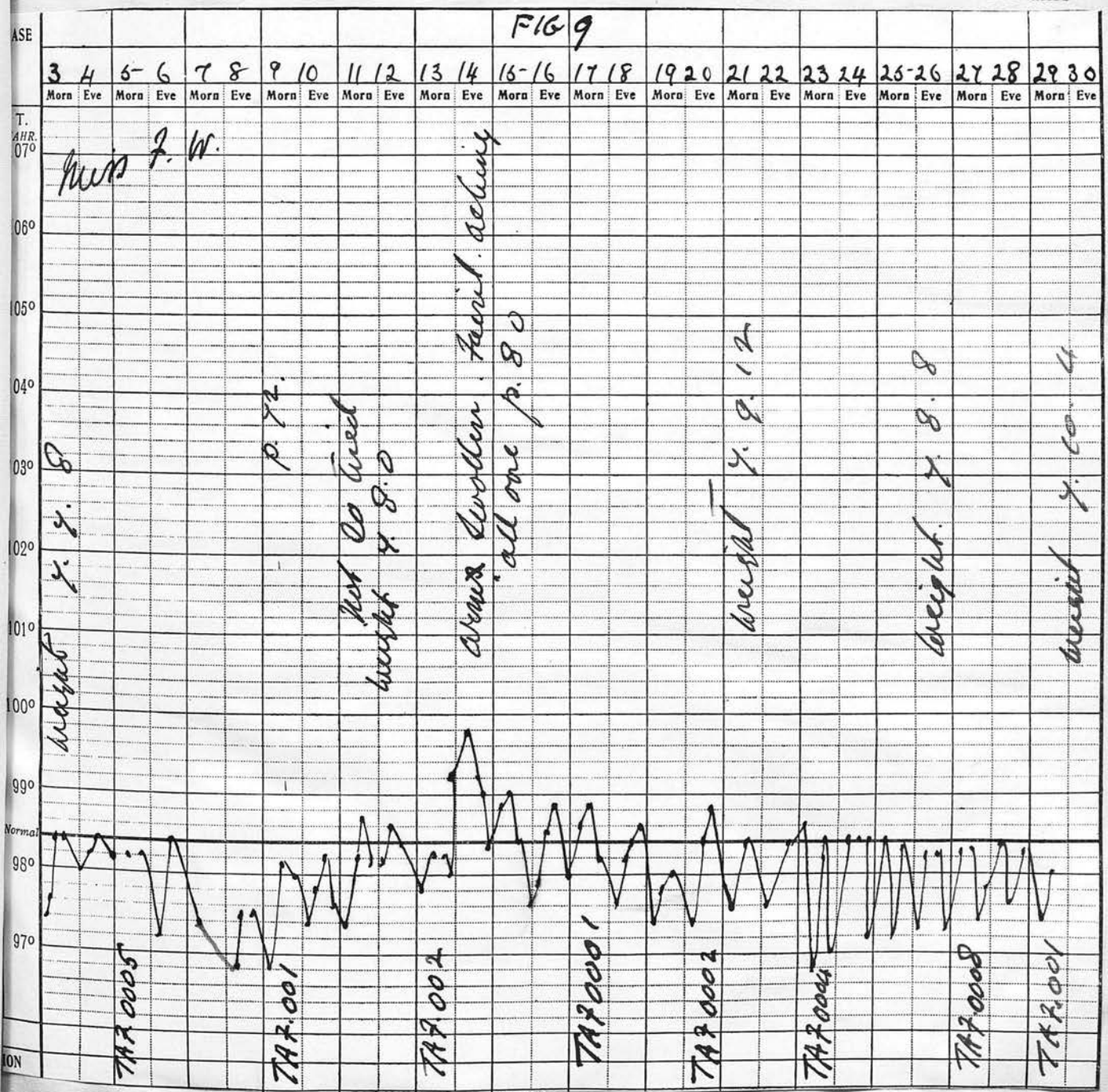
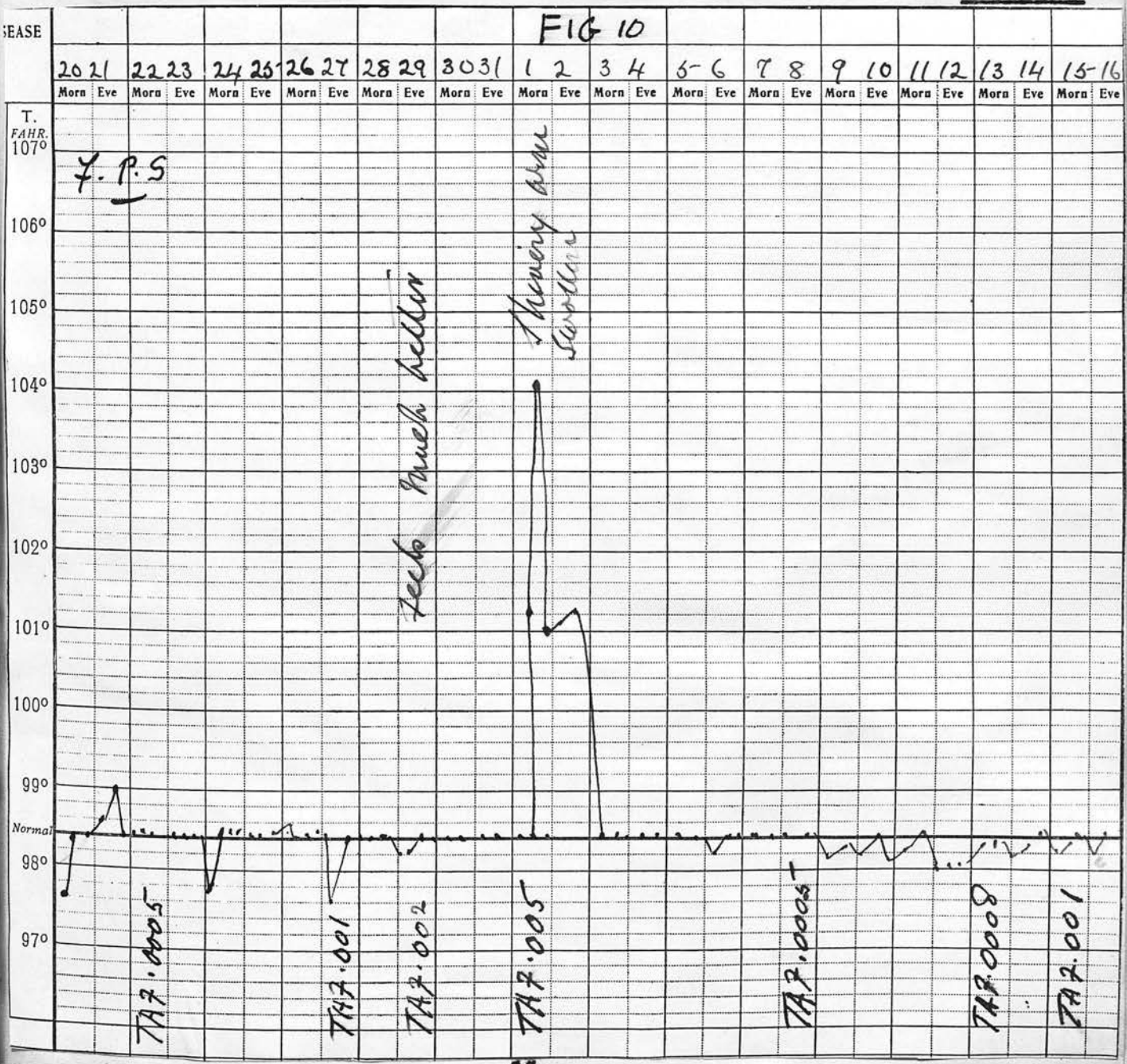


Fig. 10. F.P.S. is an example of a subsensitive case. It would have been wiser perhaps to have gone to 004 instead of 005 as the reaction was a very severe one. It, however, did him no harm, so after an interval I dropped back to .0005, but was able to rapidly increase the dosage. The man did remarkably weal and was only a short time under treatment.

FIG. 10.



It would require a much greater experience than mine before a dogmatic statement could be made as to the initial dose, but it would appear to me that a rough estimate can be made on the lines indicated above, always bearing in mind that it is better to under dose than over dose, but that at the same time the most good is done by the largest dose a patient can stand without harm.

Having fixed on the initial dose and it having been given without harm, I usually proceed in this order. Say .0001 has been given without detriment, proceed next to .00015, then 00025, then to .0004 .0006 00085 .001 and so on, judging each case on its merits. If there is any sign of hypersensitiveness give the same dose again, reduce it, or omit it altogether, according to circumstances. It is impossible to lay down rules, each case must be judged on its merits.

For instance, take Fig. 11. Part of Miss F.W's. temperature chart I was able to push the doses. There was a drop in weight on the 8th., but there was no reaction, so I proceeded with cautiously increased doses. On the 16th she had gained a pound, and on the 25th gained another pound, and was keeping well in every way. Consequently, one was able to rapidly increase the doses up to the end of the course.

FIG. 11.

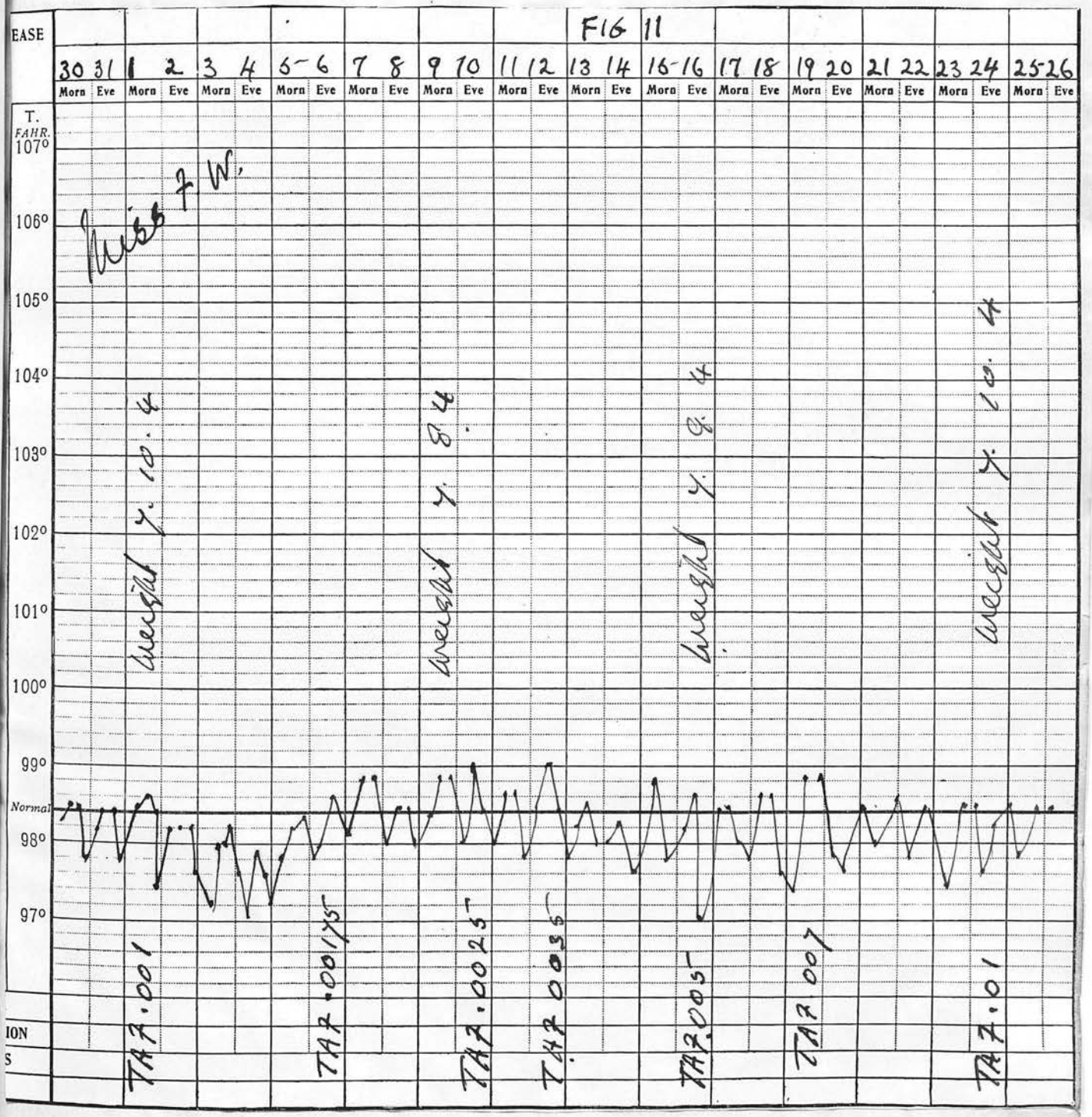

EASE
30 31 1 2 3 4 5-6 7 8 9 10 11 12 13 14 16-16 17 18 19 20 21 22 23 24 2526
Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve
T. FAHR.
107°
106°
105°
104°
103°
102°
101°
100°
99°
Normal
98°
97°
ION
S
Fig 11
Russ F. W.
weight 4. 10. 4
TAZ. 001
weight 4. 8. 4
TAZ. 00255
TAZ. 00155
TAZ. 00355
weight 4. 9. 4
TAZ. 0055
TAZ. 007
weight 4. 10. 4
TAZ. 01

Fig. 12. Part of chart of Miss E.G. There was some hyper-sensitiveness at 00035. The same dose was consequently repeated. This was obviously overdosing, as shewn by increased rise of temperature and loss of weight.

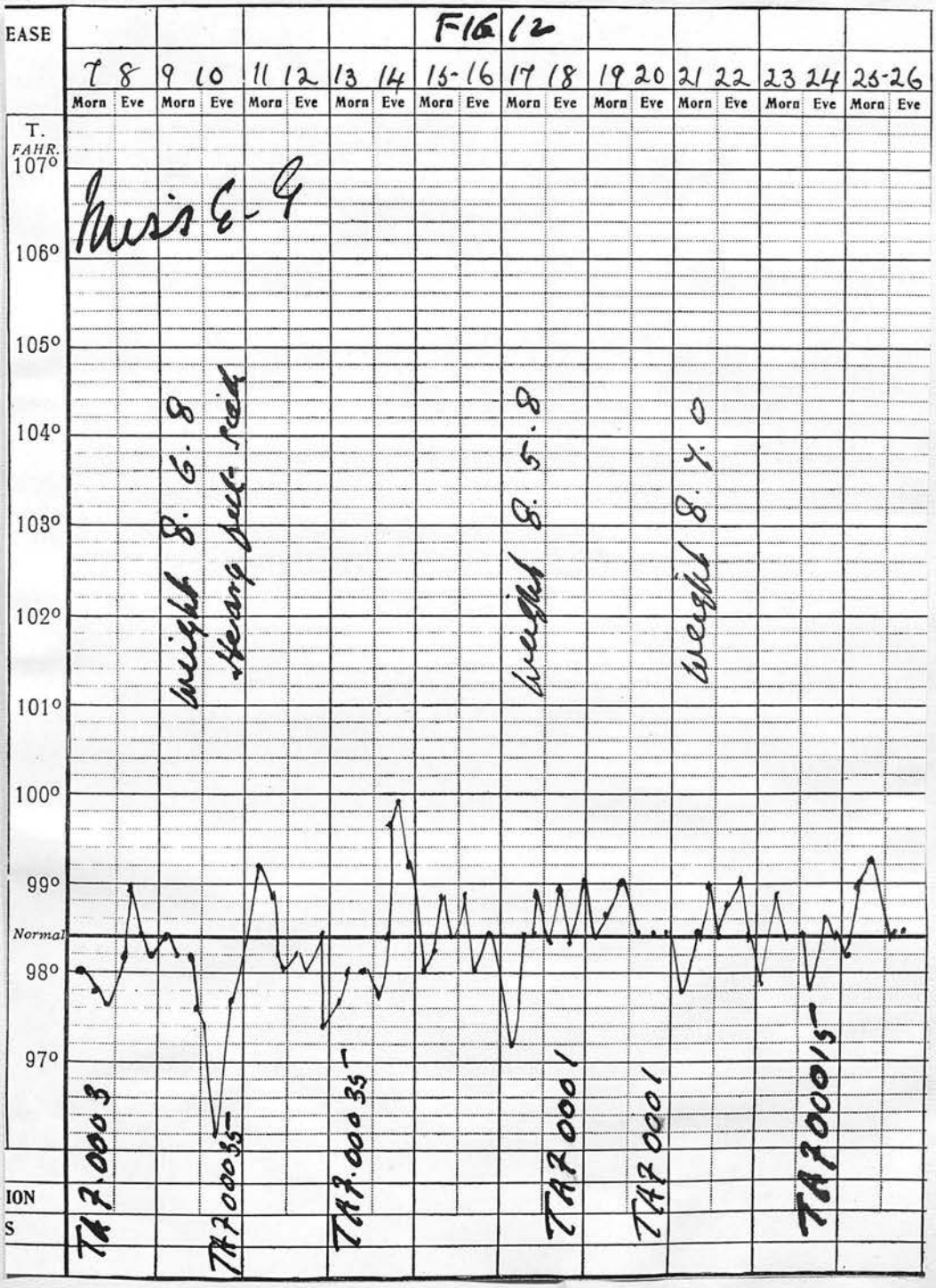


FIG. 12.

I therefore dropped to .0001 and repeated this. Note immediate rise in weight.

Since I have taken to T.A.F. and T.A.F. alone I find that I get much less severe reactions and this is all to the good. Occasionally I have had a mild reaction with O.T. (old Tuberculin) which I used to use for testing and this was followed by quite a severe reaction with a mild dose of P.T.O. I must confess I have never seen any harm follow, but it causes needless discomfort.

The Maximum Dose.

There is no definite rule as to when you should stop treatment. Cayae Wilkinson fixes l.c.c. of T.A.F. as the dose that should be aimed at and I follow his teaching, but as Sahli says, there is probably an optinium dose for the individual. When large doses are being reached it is wiser to go more slowly, for, incertain cases, hypersensitiveness is again established and it appears to be wiser to leave well alone and not press the treatment too far.

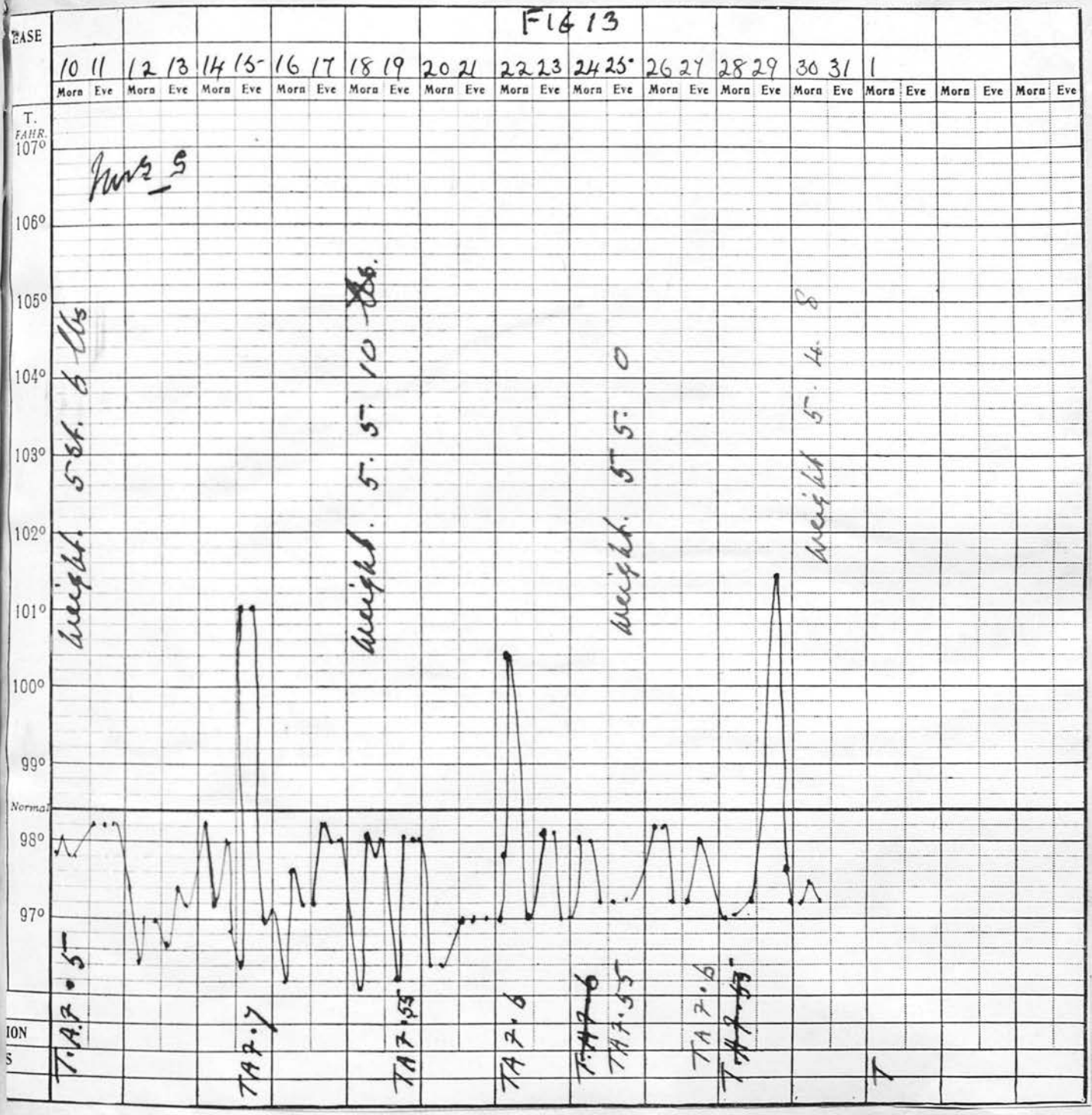
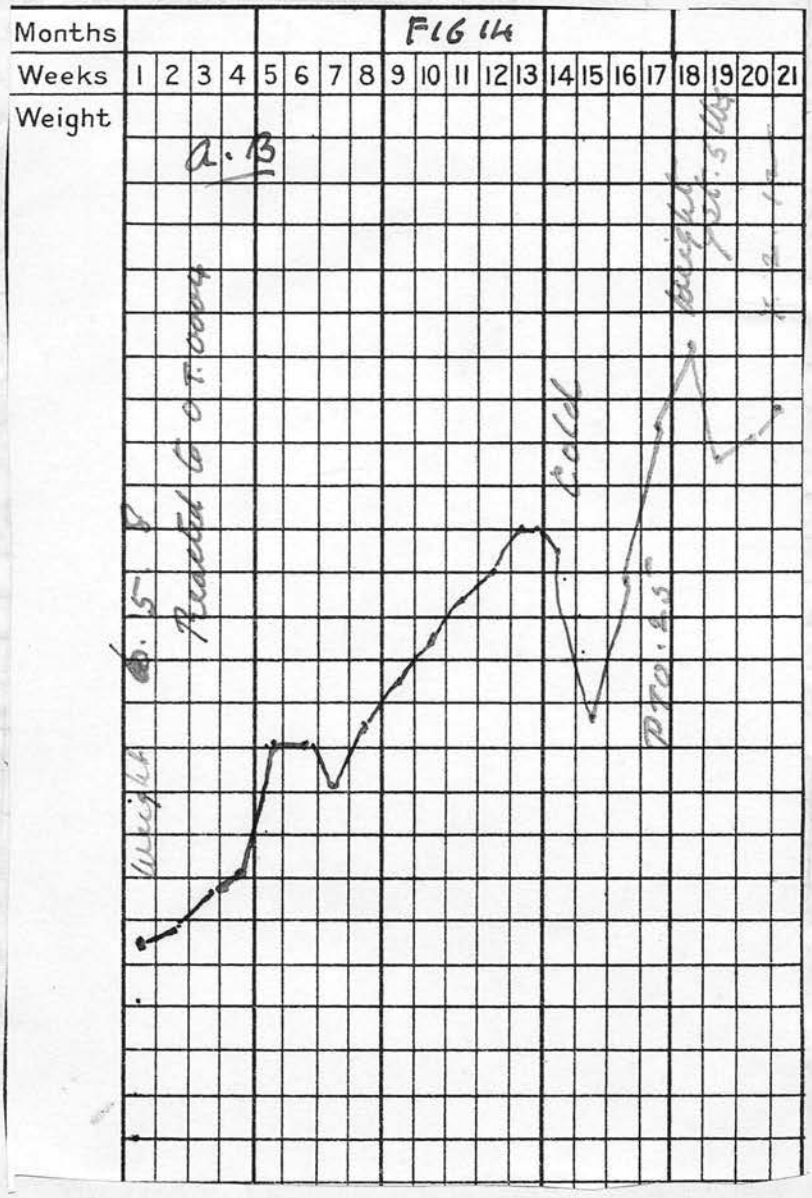


Fig. 13. Part of chart of Mrs S. is a good example of the importance of knowing when to stop treatment. She had

practically no reactions until .7 was reached, when she had a severe reaction. So I dropped the dose to .55. This had no effect. I then gave .6 This was followed by a reaction. I went back to .55; no effect. Then to .6; a severe reaction. Evidently the limit in her case was .55. As she was beginning to lose weight it was obvicusly inadvisable to continue treatment further.

It appears probable that these late reactions are due to actual overdosing, and is really poisoning with Tuberculin. They seem to be quite different in their nature from early hypersensitiveness. The early reactions seem to be due to irritation set up by the small doses. It also seems to me to explain why small doses start hypersensitiveness in surgical tuberculosis in people who are comparatively healthy, and also explains why Sahli and his school object to diagnostic tests. It is the fear that you may strike a case in which the anti bodies are insufficient to produce a reaction until a poisonous dose of Tuberculin has been given. Luckkly there is no necessity to run this risk. One realises the danger, and it is unjustifiable to test cases in whom the diagnosis can be made by other means.

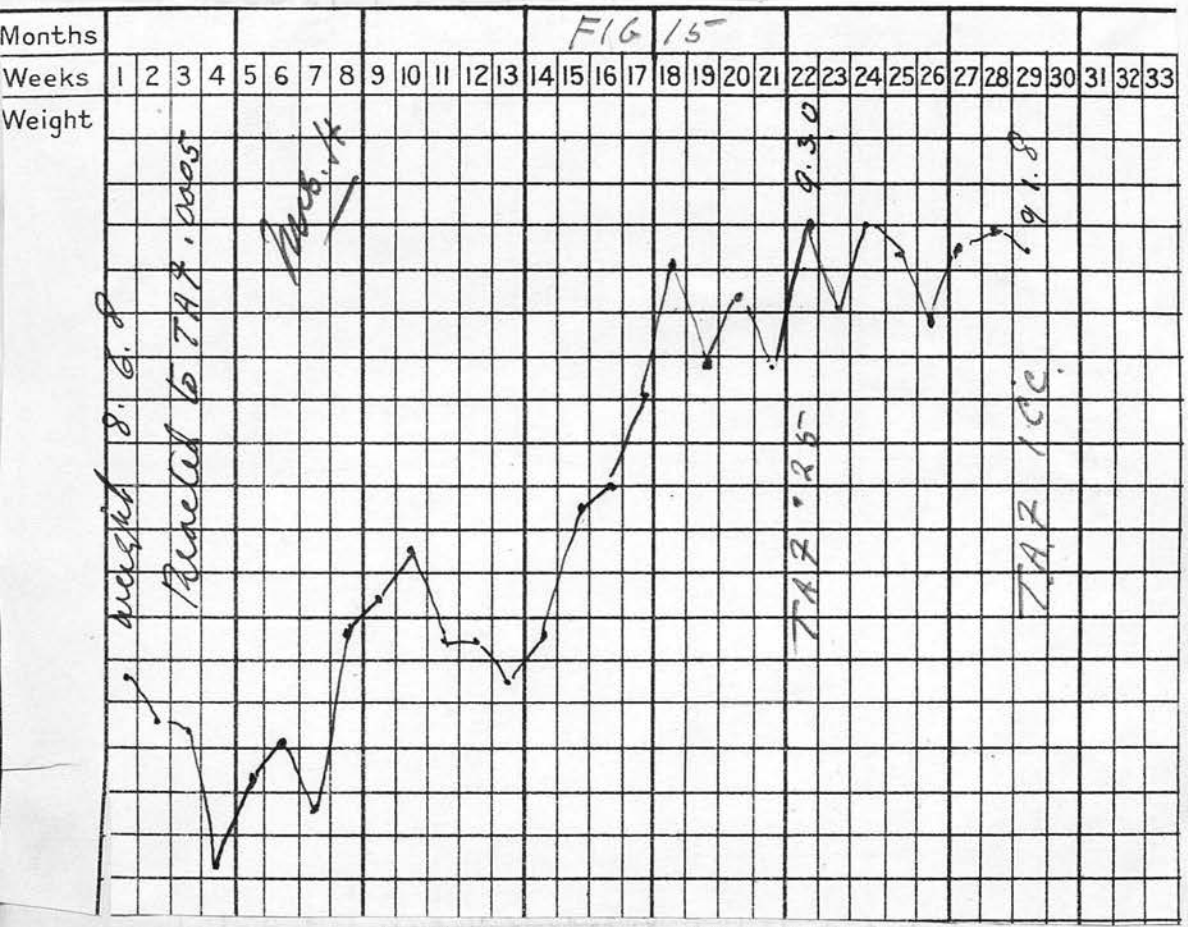
FIG. 14.



Optinium dose.

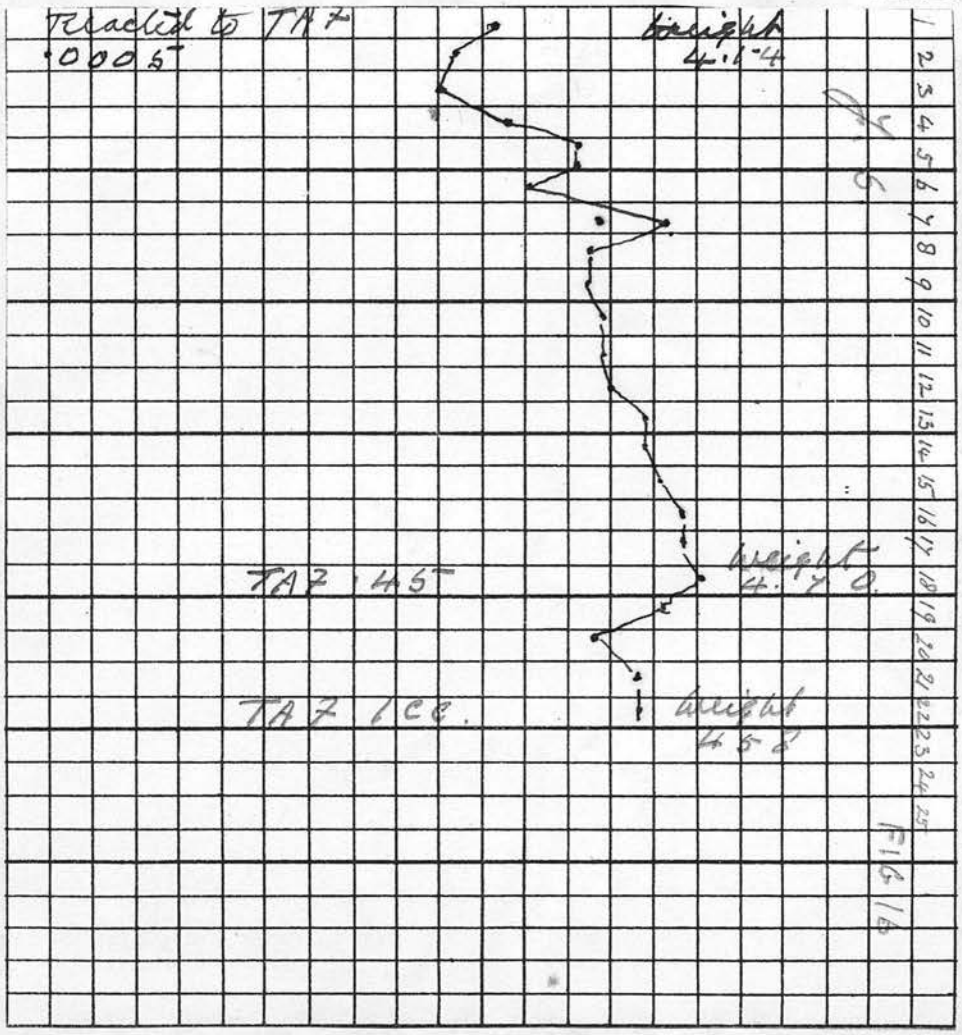
P.T.O. 25.

FIG. 15.



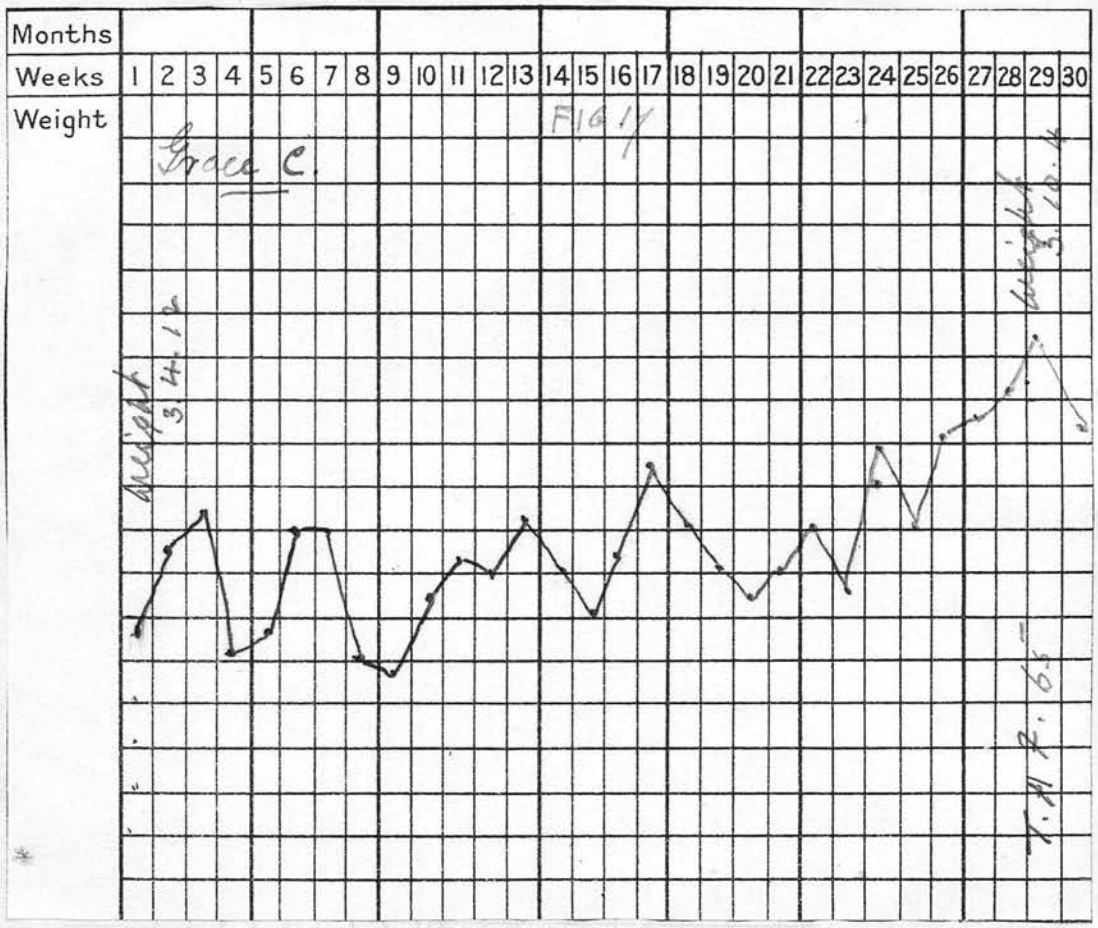
Optinium dose. 25. T.A.F.

FIG. 16.



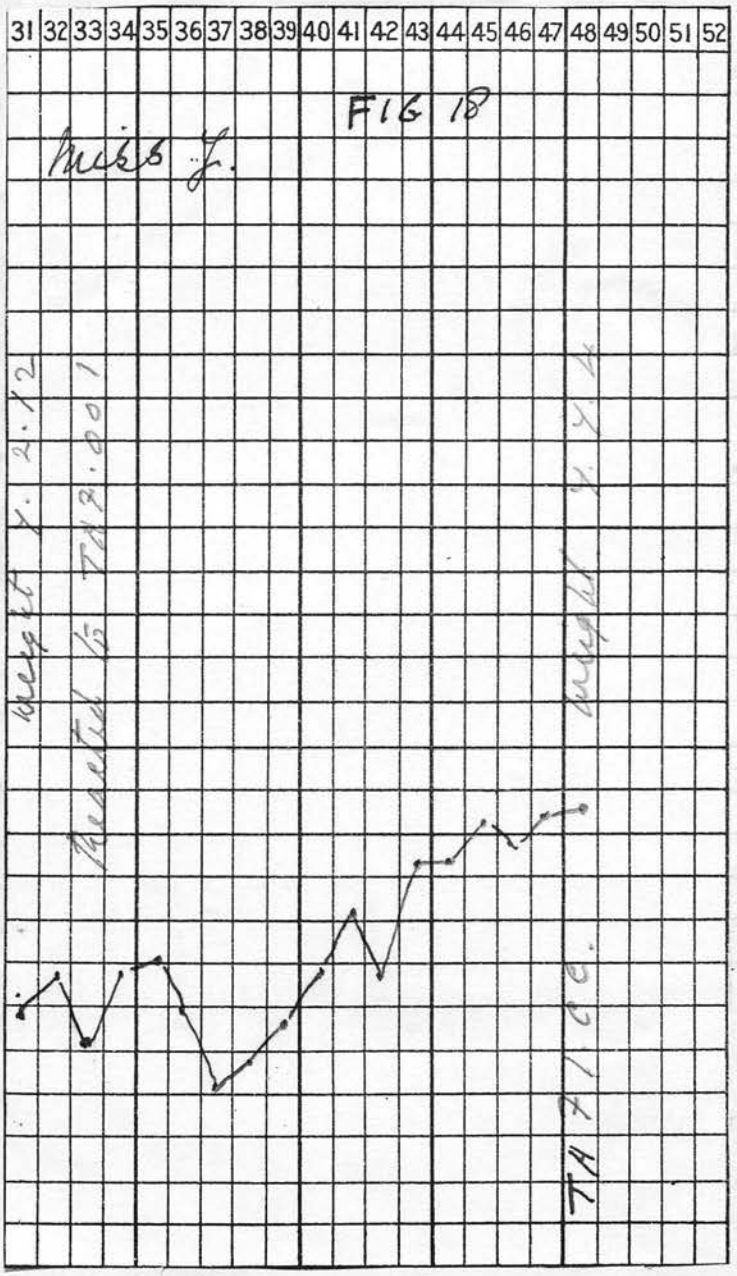
Optinium dose T.A.F. .45.

FIG. 17.



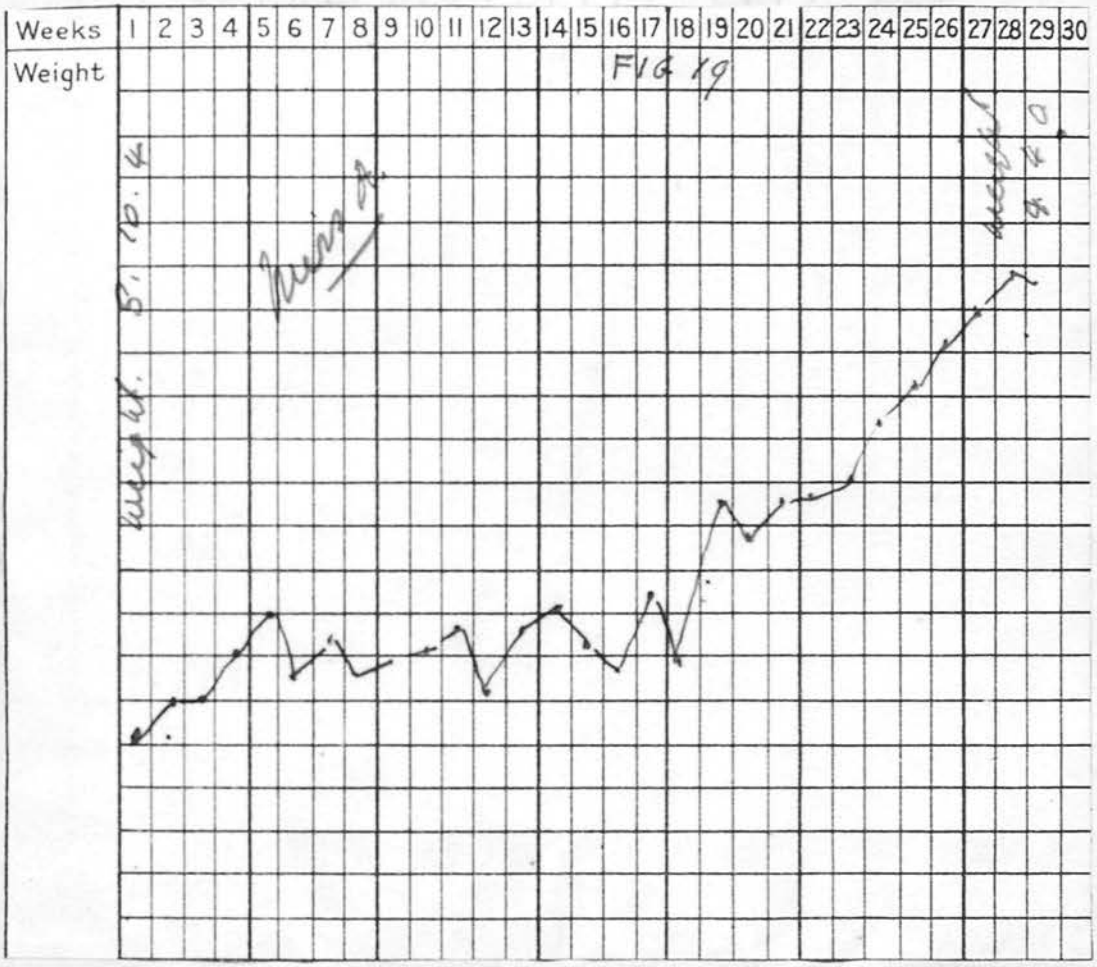
Optinium dose .65.

FIG. 18.



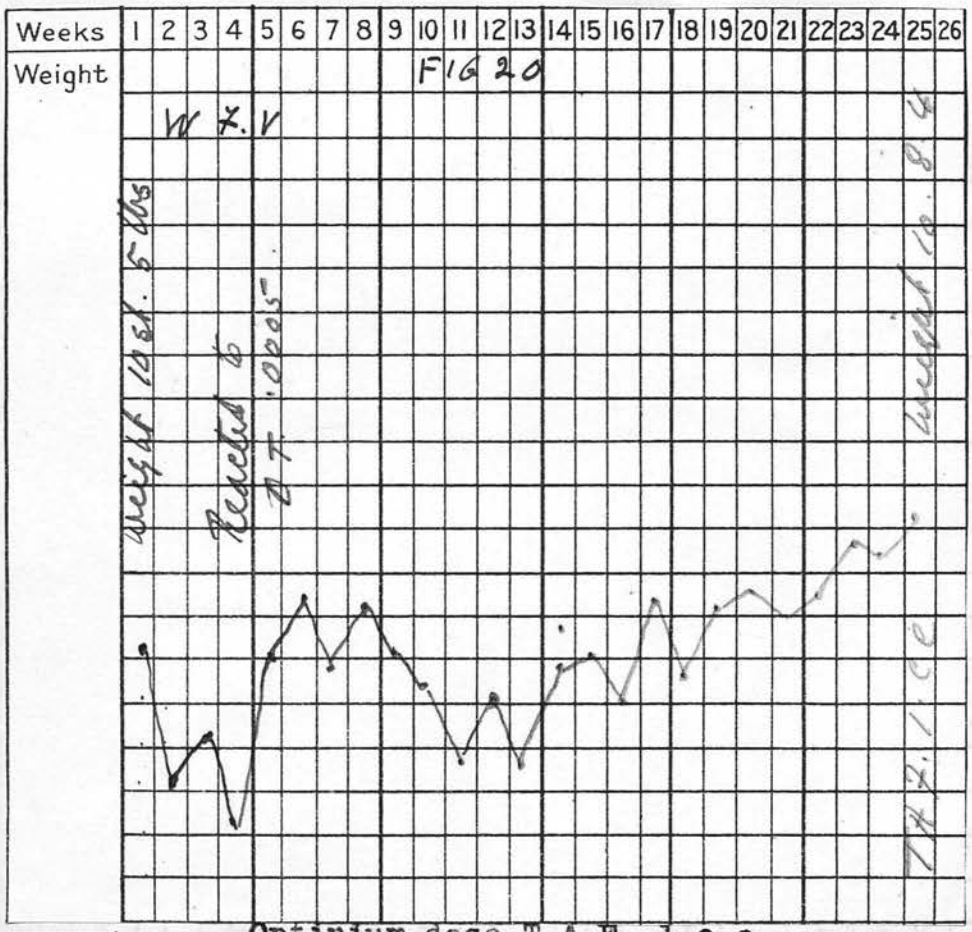
Was able to take 1.c.c. without detriment.

FIG. 19.



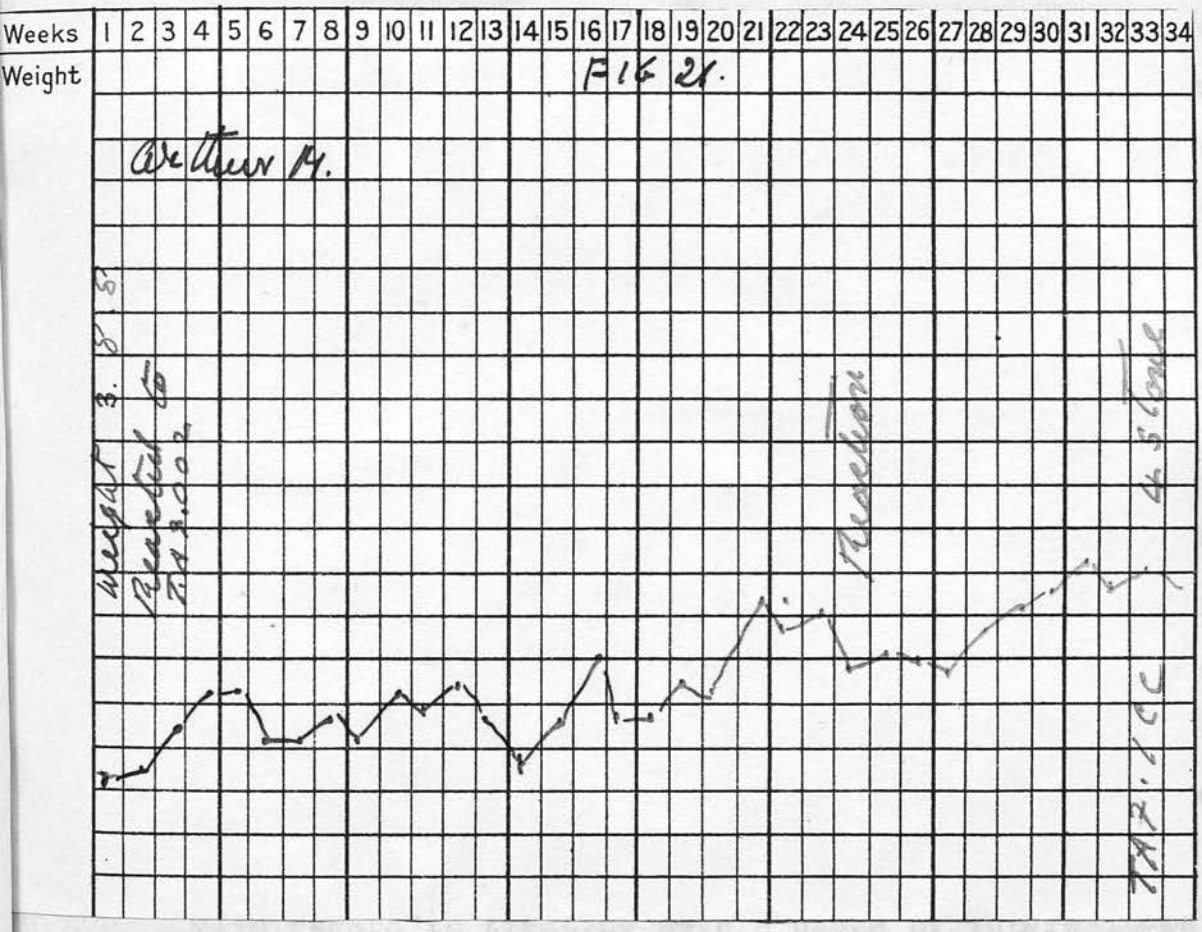
Took 1.c.c. without detriment.

FIG. 20.



Optinium dose T.A.F. 1.c.c.

FIG. 21.



Optinium dose .1 c.c. T.A.F.

Appended; Figs 14 to 21, are some samples of weight charts in patients who did well. Most of them were able to complete the course up to 1.c.c. but in a few I think it would have been better if I had discontinued when the weight began to drop a little. I do not think it is wise to insist on reaching 1.c.c. when in testing you give a person a free bill of health as far as Tuberculin is concerned if they do not react to .01 c.c. It seems illogical. Take the case of Mrs H. Fig 15. She reached her optinium weight with T.A.F. .25 and was absolutely well in herself. There seems little object in continuing further than this in such a case.

The above weight charts are samples of cases which did well on Tuberculin. But there is a reverse side of the picture, and it would be possible to give examples of cases in which it certainly did no good, but possibly harm. However, if one bears in mind the all-importance of hypersensitiveness and toxaemia, one should not make many mistakes.

With regard to treating severe cases of Tuberculosis with pyrexia, I agree with the teaching of Sahli and Camac Wilkinson. Tuberculin should be avoided for the time being. Baedelier and Ropke advocate it in small doses. I have tried it repeatedly, but it seems to me to serve no useful purpose and it may do harm.

It is far better to treat the case in such conditions on general principles, and if a mixed infection is suspected

to deal with this with a vaccine. A catarrhal condition should always be dealt with. For this I find nothing better than a detoxicated catarrahal vaccine manufactured by the Genatosan Company. It consists of:

Pheumocacci 15,000 millions; M. Catarrhalis 12.600 millions; B. Fiedlander 5,000 millions; B Septus (Hofmann) . 5 millions; Staphylococci 5,000 millions; Haemolytic Streptococci 2,500 millions; B. Lufluezae (Pfeiffer) 5,000 millions per cc 50,000 millions.

The initial dose as recommended by the manufacturers is far too high for tuberculosis cases. They recommend .1.c.c. You can get a violent reaction with a much less dose than this. I had one case which reacted to 102 with .01 of this vaccine. However, it is usually safe to begin with .01 and double up .02; .04; .08; and then to go more slowly and get it more on Tuberculin lines .1; .15; .25; and so on.

It can well be combined with Tuberculin, as is seen in the chart of Miss P. Fig. 16.

As just mentioned, however, even with a detoxicated catarrhal vaccine, given in small doses, you may occasionally get a violent reaction, as seen in the case of D.A.P. Fig 17.

FIG. ~~16~~

The Chart of Miss P.

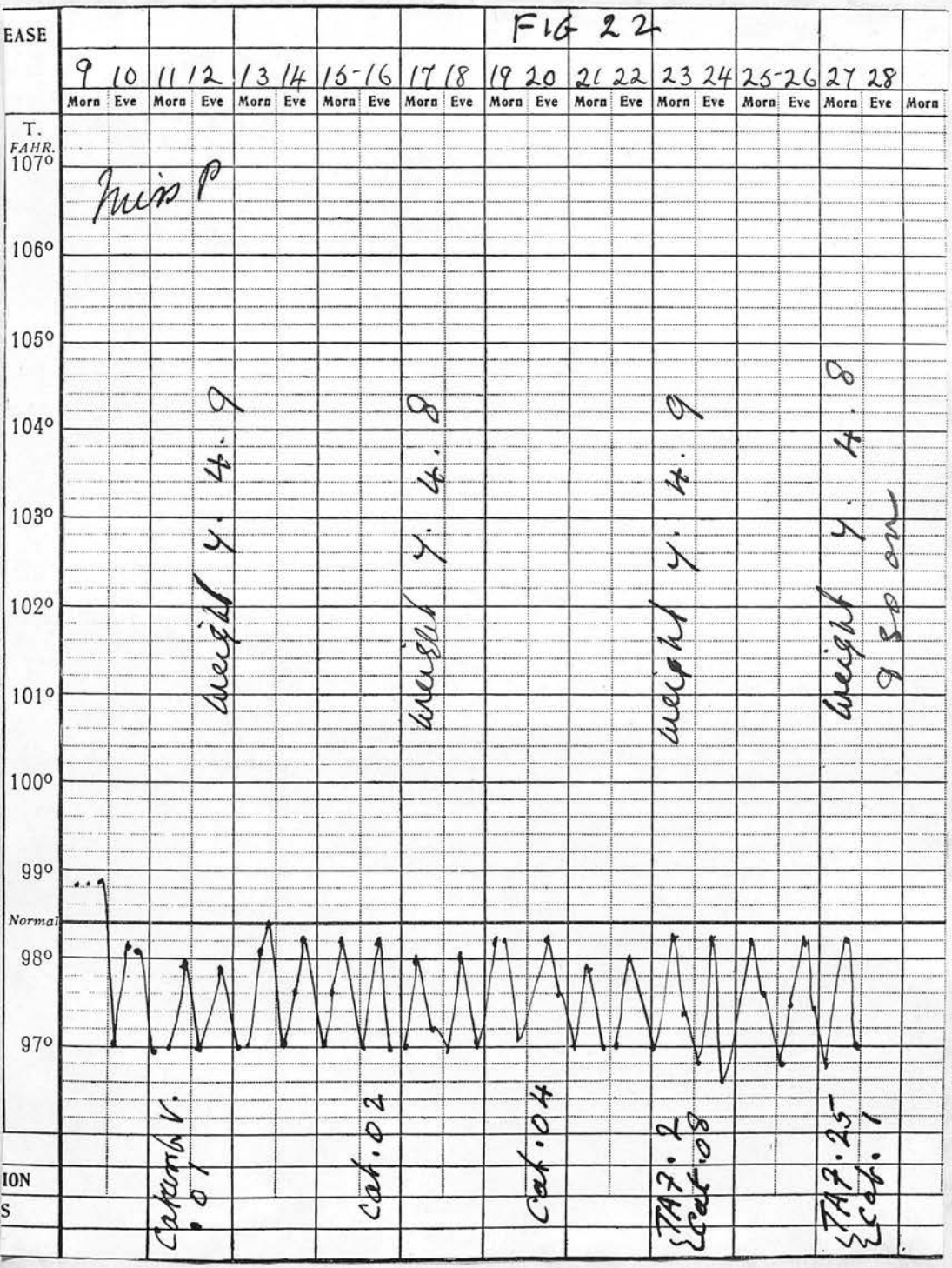
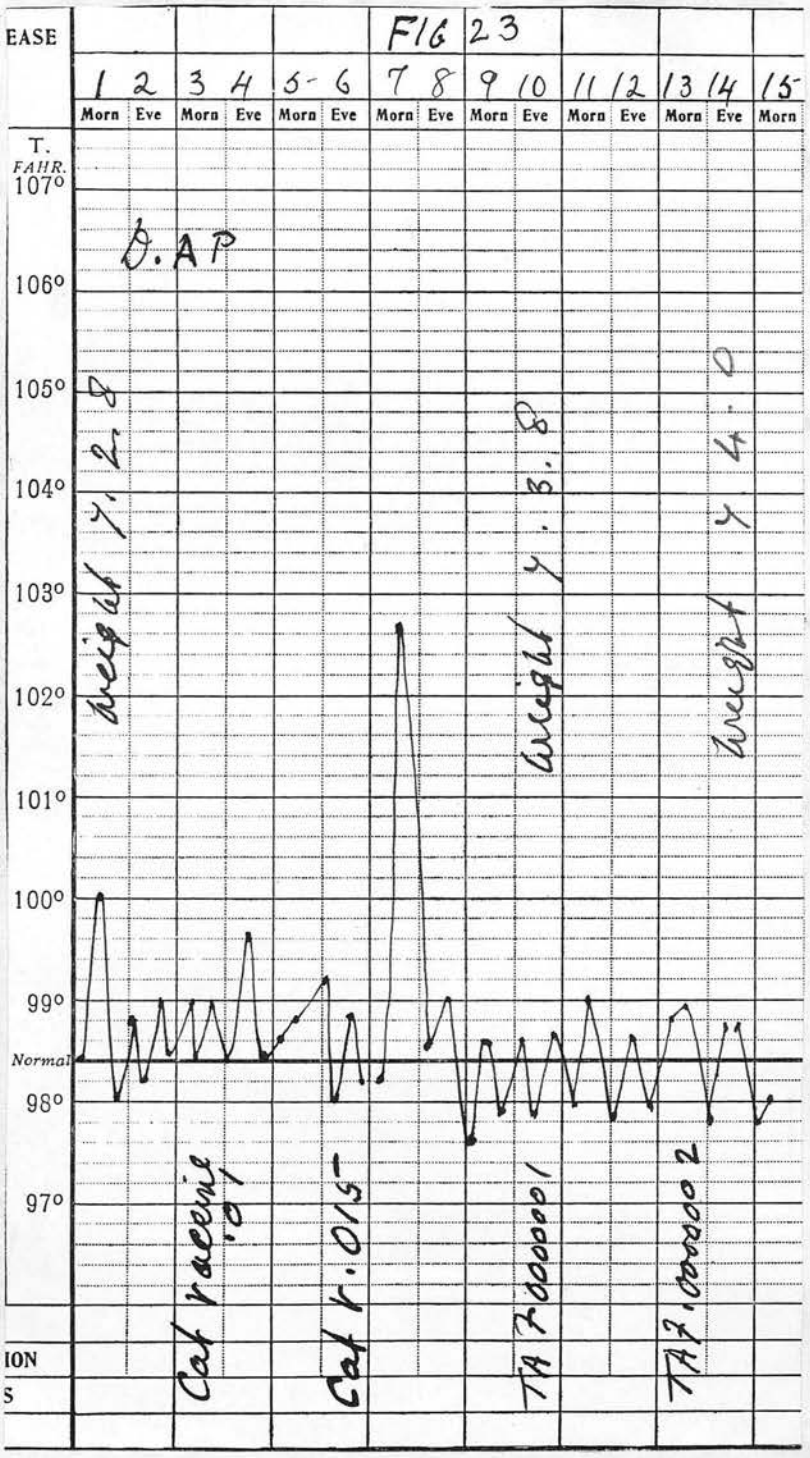


FIG. 12.



The Case of D.A.P.

In such a case it is advisable to discontinue the vaccine.

Ordinary coryza vaccine as supplied by Messrs Parke Davies should be used with the greatest caution as to dosage in tuberculosis. I have had this brought to my notice very markedly lately. At Margaret Street we have the care of officers suffering from tuberculosis under the Ministry of Pensions. At the request of other members of the staff I have undertaken to give "vaccines for colds" to such officers as required this treatment. I find that even with .1 of a c.c. the reaction is sometimes exceedingly violent and is followed by a loss of weight. I treat this vaccine now in the tubercular with considerable respect, and prefer in most cases to use the detoxicated vaccine described above and to give in very graduated doses. I use it very considerably in cases of high temperature with benefit when it would be quite unsafe to use Tuberculin.

REVIEWS OF CASES I HAVE TREATED WITH TUBERCULIN.

Introductory.

When you are approaching a difficult subject in a critical attitude the only way is to attack it as an enemy to your pre-conceived ideas.

It would be easy, by taking favourable cases only, to write up Tuberculin as the cure for all ills. It would be equally easy to select unfavourable cases and condemn it in like manner. This method has been freely used, with the usual result - chaos. If anyone could write a treatise on when to use Tuberculin and when to avoid it the problem would be simple. Till this problem has been solved scientifically nothing can be done. All the ordinary man can do is to go cautiously and record his results. What I propose to do is to give a frank account of my cases, and to acknowledge my errors as they are apparent to me.

Sahli rightly points out that in order to give Tuberculin rationally, you must have a theory as to its action. Otherwise, you are working empirically and you give dose after dose as shots in the dark, only pulling up - perhaps too late - when you have done definite harm.

As a result of reading, thought, and study of my own cases, I have formed a working hypothesis, which, though it may be a wrong one, has helped me considerably with my later cases.

It is based on hypersensitiveness. Without going into the question of the mode of infection in tuberculosis, which is without the purpose of this thesis, I take it for granted that the great majority of mankind have in childhood acquired tuberculosis, but that the body cells have been sufficiently powerful to prevent the spread of the disease.

Pottinger, quoting Hamburger, says that there is progressive increase of children who react to Tuberculin from the 2nd to the 14th year. In the 2nd year only 4 to 9% react. This mild infection in children may actually be a provision of nature: the mild infection may have established sufficient anti bodies to antagonize the mass infection to which the child may be constantly exposed. Such children will resist the introduction of more Tuberculin, which they show by hypersensitiveness.

I object to the assumption that hypersensitiveness denotes activity. Were this so the severity of the condition would be comparable to hypersensitiveness. You could say that the condition was more serious, when using a modified

Von Pirquet, with a reaction of 1 in 500 than 1 in 100, but this is certainly not so.

For instance, in the case of Lucy C. She reacted to 1 in 500, but no abnormal physical signs were detected and the Skiagraphist's report was "lungs apparently normal." So In the case of"glands"and lupus; these are often very hypersensitive, but the conditions are not serious as reggrds life.

Camae Wilkinson says that if you want to produce hypersensitiveness you will give a minute dose, and that after a considerable interval, say, a week to ten days, you will give another minute dose.

What I think happens is that the small dose acts as an irritant; there is not enough Tuberculin in the body to assist, and consequently there is a severe fight between the injected Tuberculin in the body and the anti bodies. In ten days time the Tuberculin has all been used up, but the inflammation of tissues has not subsided and therefore a fresh dose of Tuberculin injected, acting on inflamed tissues, causes more reaction than before. Supposing, however, you repeat the dose of Tuberculin in, say, three days - then this extra Tuberculin causes a reinforcement of anti bodies to come to the assistance of those already fighting, and the tubercular toxin is neutralized without a fight, that is without a severe reaction. That something

of the kind takes place I feel certain. Otherwise I do not see how repetition of the same small dose can lead, in the end, to improvement without reaction, which is often the case. With gradually increasing doses, more and more anti bodies are formed and if the Tuberculin is not in excess the Tuberculin balance is maintained and there is reactionless progress.

Wilkinson says "never double; if you do you may get a severe reaction." I have proved the wisdom of this many a time, and it is quite compatible with my "Tuberculin Balance" theory. As time goes on, and as the anti bodies are getting stronger and more numerous, you can safely push your Tuberculin for the anti bodies are strong enough to deal with it. When, however, you are getting to really big doses, say, anything above .01 c.c. which is taken as the limit dose for the Tuberculin test, you may be putting in more Tuberculin than it is possible for the individual to deal with, for I take it that the formation of anti-bodies must be limited, and that the limit in some individuals is reached sooner than in others. You then are up against Tuberculin poisoning. There is more Tuberculin in the body than the anti bodies can deal with. In this way you are directly harming your patient. This Tuberculin balance theory seems to me to explain why in testing old cases of

tuberculosis you have to push the test to, say, 001 or 002. The disease itself has already established sufficient anti bodies to deal with the Tuberculin up to that extent. It also explains why minute doses of Tuberculin apparently have no effect in severe tuberculosis. More than sufficient Tuberculin is already being formed. It also explains how a large dose in such a case may easily kill. I take it, then, that the main use of diagnostic tests is, not to ascertain the extent of activity, which can be found out more efficiently by other tests, but as a test of hyper-sensitivity, and, as such, a guide to dosage.

Wright (Studies in Immunization) reports a remarkable case of a woman with lupus, who, as a result of gross overdosing with Tuberculin, lost her left arm. She came into his hands some years afterwards and by gradual immunization with small doses, he restored her to comparative health. This was obviously a case of Tuberculin poisoning in a woman with powerful resisting powers.

It may be asked what is the justification for testing people when the reaction is so universal. I disarm criticism by saying: "none, if you can make your diagnosis by other means," but the more I see of the disease the more I am convinced that obscure symptoms are frequently due to a tuberculin toxaemia, and that when you have decided that this is

the case, by ascertaining the degree of hypersensitiveness present, then you are better able to treat your patient on rational lines.

Does hypersensitiveness explain the harm of giving Tuberculin in a mixed infection? I think it does. Let it be granted that the catarrhs, for instance, of tuberculosis of the lungs are more or less an acute condition, and let it be granted that Tuberculin is an irritant. It follows that inflammatory action must be increased and the catarrh rendered worse.

Working on the above hypothesis then, my present methods are as follows.

I make my diagnosis by other means if possible. Failing that, I test with Tuberculin, being satisfied with the smallest local, focal, or general reaction. I then treat the case, beginning with the highest dose that the reaction appears to permit; increase my doses cautiously; then more boldly, till there is an indication that I am getting near the optinium dose, and then proceed very cautiously for fear of late poisoning.

I am aware of the pitfalls in my theory, but it has proved of service to myself, and I give it for what it is worth.

Classification of Cases.

When one is dealing with a limited number of cases it is questionable if a definite classification is of much service.

It is obviously useless to divide them into surgical and medical tuberculosis, as the latter in my practice so greatly predominates.

It also appears unsound to classify according to the physical signs detected in the lungs, for that depends very much on the skill and acuteness of hearing of the observer.

It appears to me that the simplest classification for my purpose is to group the cases according to their sensitiveness to Tuberculin, and I have, accordingly grouped them into three main groups: A - Hypersensitive. B - Sensitive. C - Subsensitive.

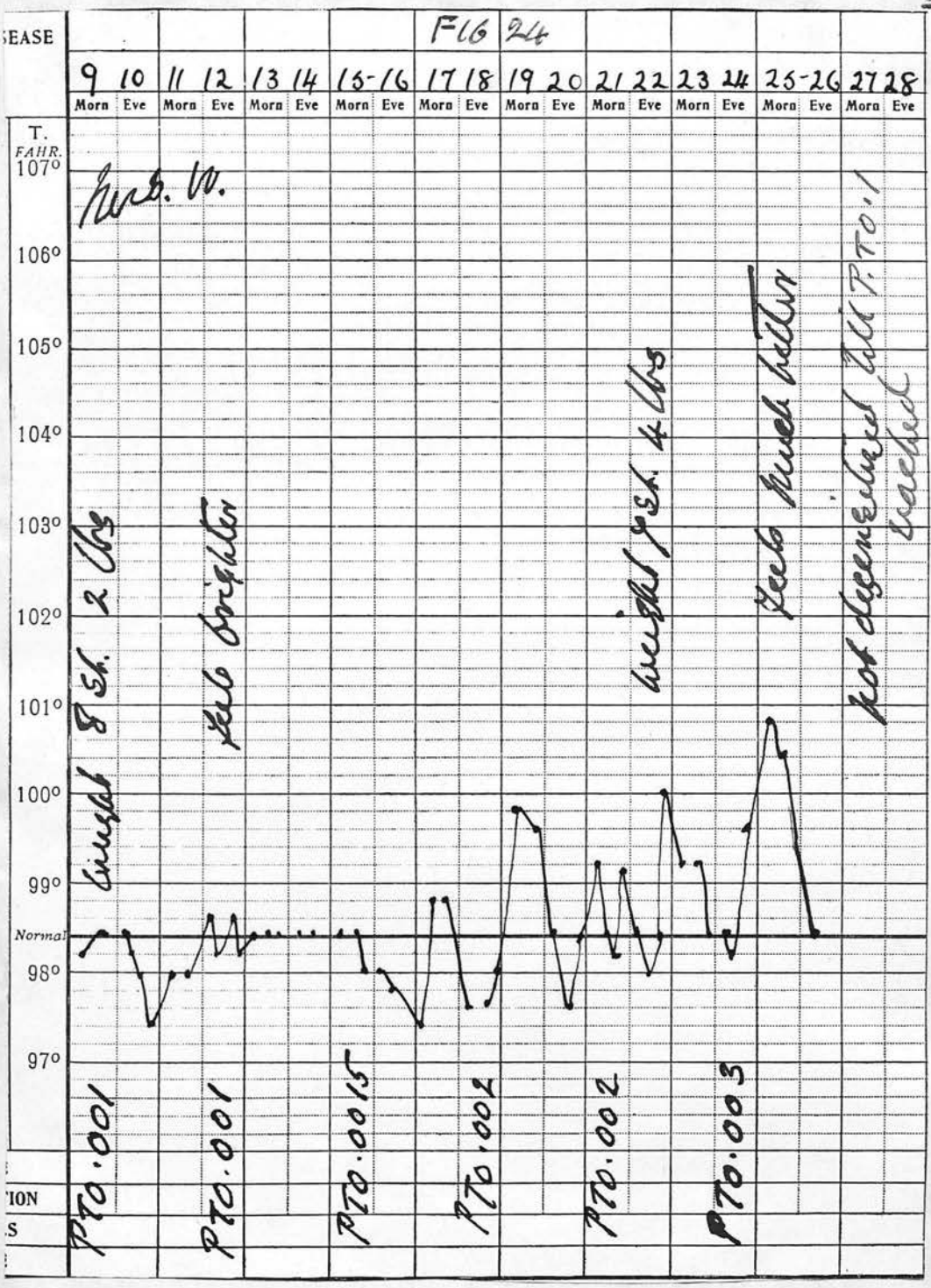
Additional groups are: D. - Those with T.B, in sputum. E. - Miscellaneous. F. - Hospital Cases.

Cases Reacting to .0005 and Under.

1. Mrs W. 32. Saw first 24. 3. 20.* History: Feeling weak for some time. States used to spit up blood. Night sweats. Breathless. Miscarriage last November. Brother died of Phthisis. Physical signs: Systolic at apex. Increased vocal fremitus right apex.
Weight 8st. 2lbs. Reacted to 100 to O.T. 0005. Commenced treatment with P.T.O. 001. Then P.T.O. 0015 with slight reaction. P.T.O. 002 produced shivering headache and slight cough. Reaction to 100. I repeated the dose next time with the seame result, I then went to 003; savere reaction but felt better, and so on. Had reactions till P.T.O. 1 reached. After this more/or, less reactionless. Treated with P.T.O. up to 1.cc, then P.T. up to .25 cc, then O.T. up to 1.cc.
Result. Finished Dec. 20th. 21. Feels very well.
Reported Sept. 21. '21. Absolutely well in every respect. Gained 10 lbs.

The dosage in this case was pressed far too much for a sensitive case. Notice the considerable loss of weight for a time.

FIG. ~~18.~~

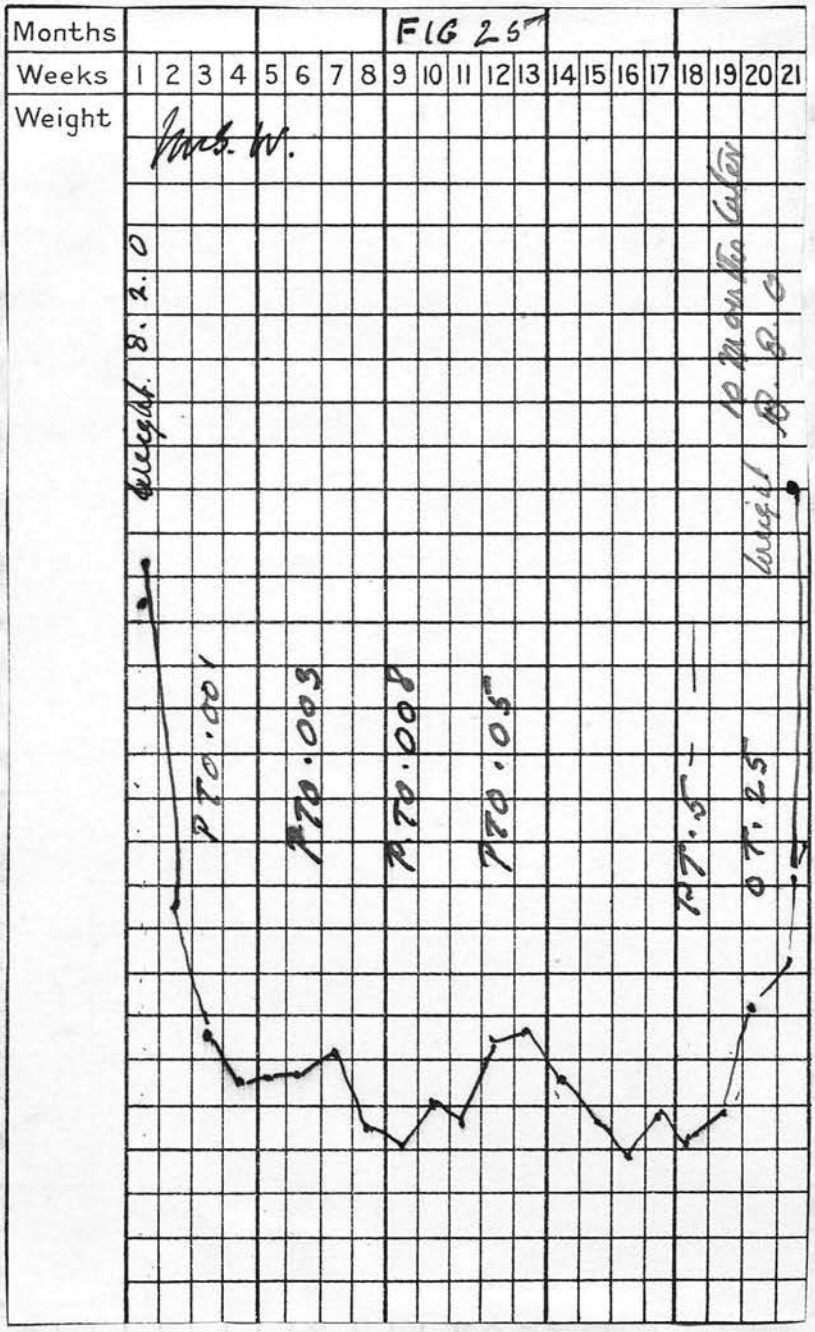


Mrs W.

94.

25

FIG. ~~19.~~



Mrs W.

2. E.W. 6 Years. Son of Mrs W. 17. 6. '20.

Cough for twelve months. Fever, night sweats. Thin.

Nothing special in lungs. Enlarged tonsils.

Tested with O.T. .0002. Increased amount of expectoration.

O.T. .0004, reacted to 101°.

Commenced treatment with P.T.O. .0005. Severe reaction.

Repeated dose. No reaction. Treated with P.T.O. up to .8 cc.

He seemed then in a stationary condition and in really very good health. I tried him with P.T. but this did not suit him.

His optinium weight was 2. 13. 0., after P.T.O.·13.

Reported again twelve monghs later. Weight 3. 4. 8. Apparently very well.

This case appears to bring out the importance of not pressing dosage beyond the optimum for that patient.

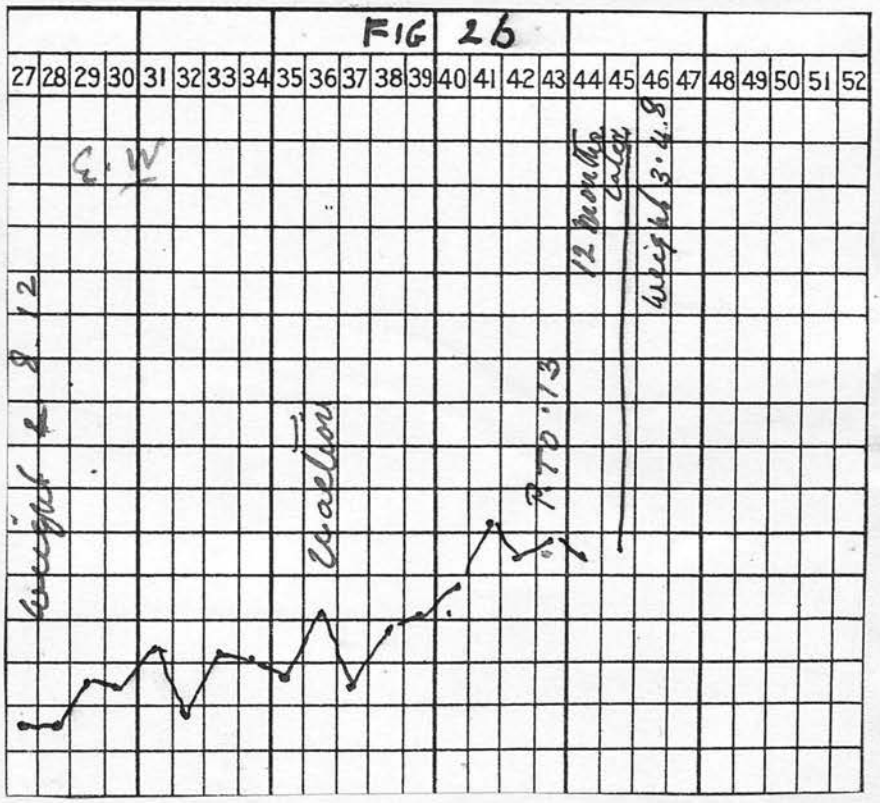


FIG. ~~20.~~ 26.

E.W.

3. Miss Z.P. 37. 28. 12. '20.

History. Diarrhoea and sickness one week, before that for six weeks off colour and low down. No appetite. No cough. No night sweats. Pleurisy six years ago. Brother died of phthisis. Glands in neck enlarged.

Physical signs: Harsh breathing below clavicle both sides. P. 100. B. Pressure 130. Hb 90%. Coagulation time six minutes.

Reacted to 100 .4 with O.T. 0005. Aching in back and head. Slight local reaction.

After 10 days given P.T.O. 0005, reaction, but feels better. Dose repeated twice. At third dose temperature normal.

It would be tedious to follow her case through, but I give a specimen of an early portion of her chart. I treated her with P.T.O up to .1 cc. I then put her on to P.T. . and later on tried her with a detoxicated vaccine. With this she did not get so much local reaction, but she still suffered from general reactions. She was a markedly hypersensitive case, reacting most violently to a wasp sting during the summer.

FIG. 21.

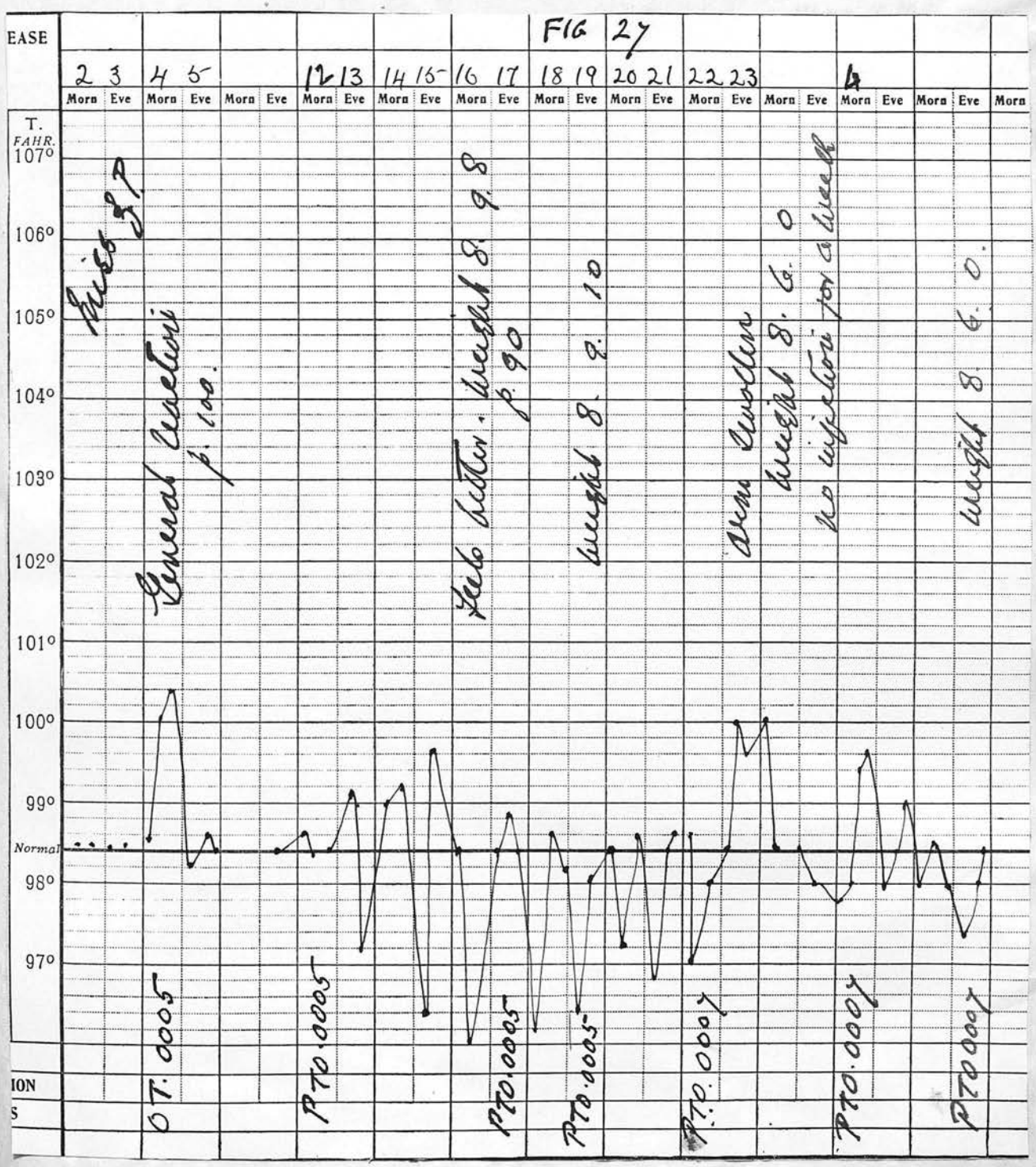
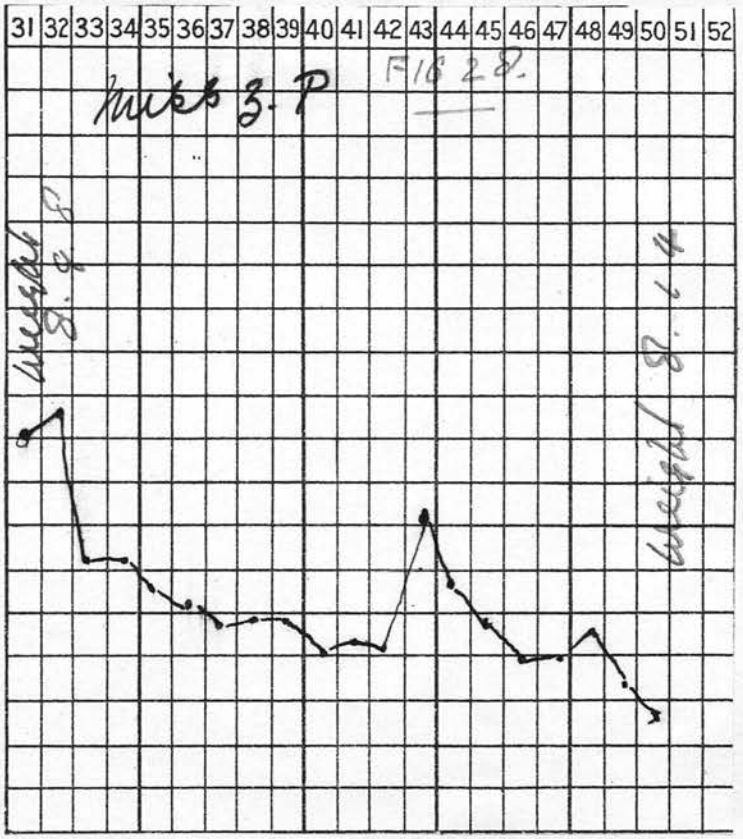

EASE
FIG 27
2 3 4 5 12 13 14 15 16 17 18 19 20 21 22 23 4
Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn
T. FAHR.
107°
106°
105°
104°
103°
102°
101°
100°
99°
Normal
98°
97°
Bisc 8.P.
General Anesthesia p. 100.
O.T. 0005
Pale Letter. Weight 8. 9. 8 p. 90
PTO. 0005
Weight 8. 9. 10
PTO. 0005
Acute Cystitis Weight 8. 6. 0 No injection for a week
PTO. 0005
Weight 8. 6. 0.
PTO. 0005

FIG. ~~27~~ 28

Miss Z.P.

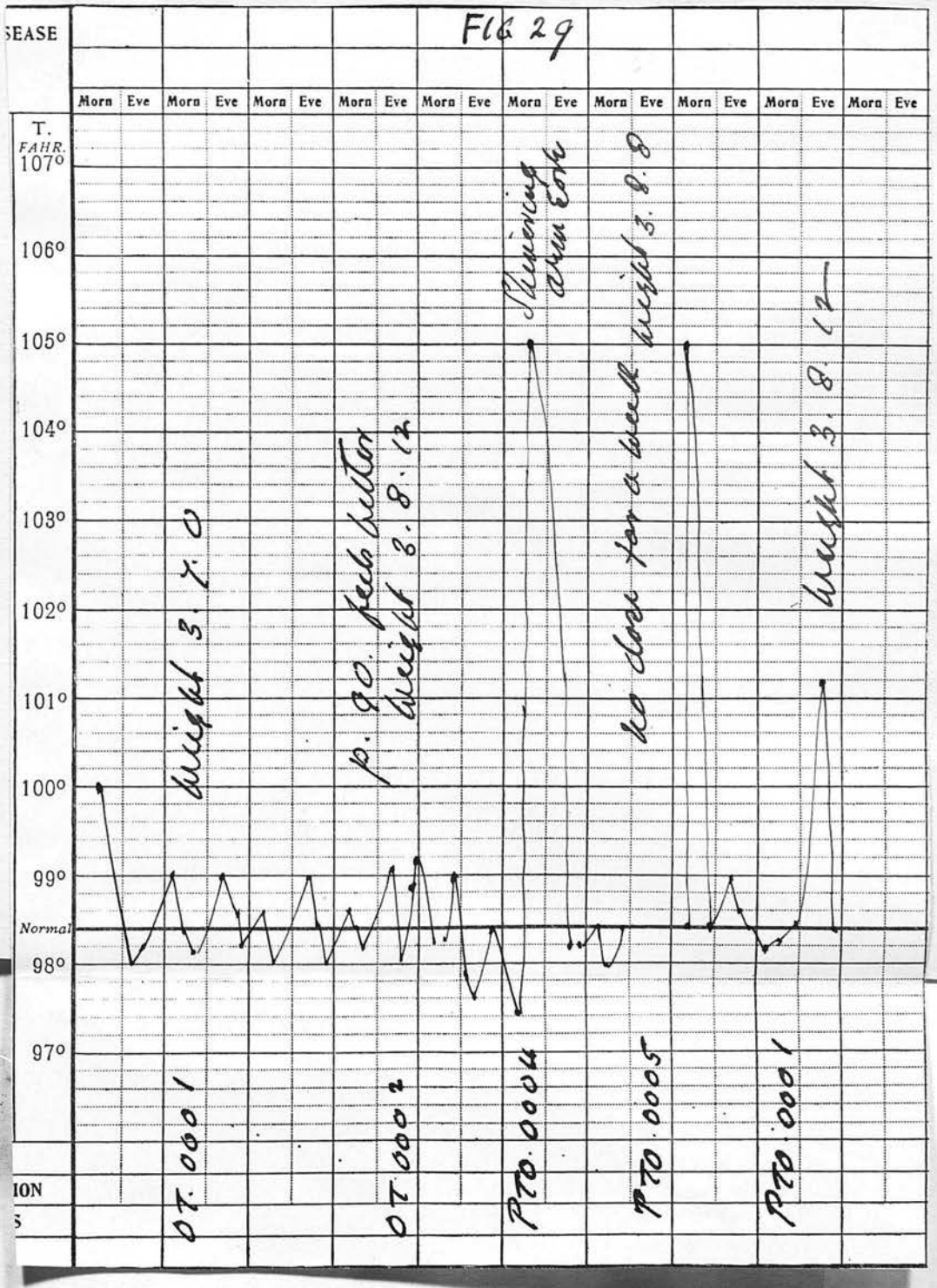


I am not at all proud of this case. She expressed herself as feeling better, but the drop in weight is not consistent with good treatment. I should have gone much more cautiously into the dosage than I did.

4. A.M. Aged 8. A nervous little boy. Off colour. Tonsils enlarged. Adenoids. Liver enlarged. Nothing to detect in lungs. B.P. 80. Haemoglobin 70%. Clots in 6 minutes. Reacted to .0002. No marked rise of temperature, but felt much brighter. In three days gave P.T.O. .0004 reacted to 105. After a week gave .0005, reacted severely. Again dropped to P.T.O. .0001, reacted, but after P.T.O. .0002 had no further reactions. Treated up to P.T. O. .5.

29

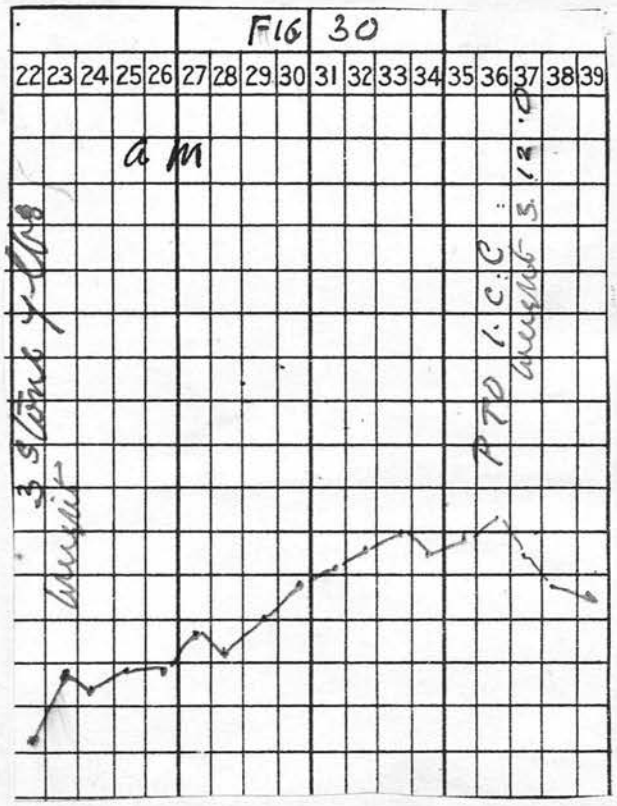
FIG. 23.



30

FIG. ~~24~~.

A. M.



The special feature in this case was the severe reactions with P.T.O. after having had practically no reaction with O.T. This is uncommon, but it occasionally occurs and is one of the reasons I dislike changing a preparation. In spite of the reactions, he steadily gained weight, and did well up to P.T.O. 1. After this he began to show signs of toxaemia.

5. M.C. Age 6. Colds. Night sweats. Lost weight.
15. 3. '21.

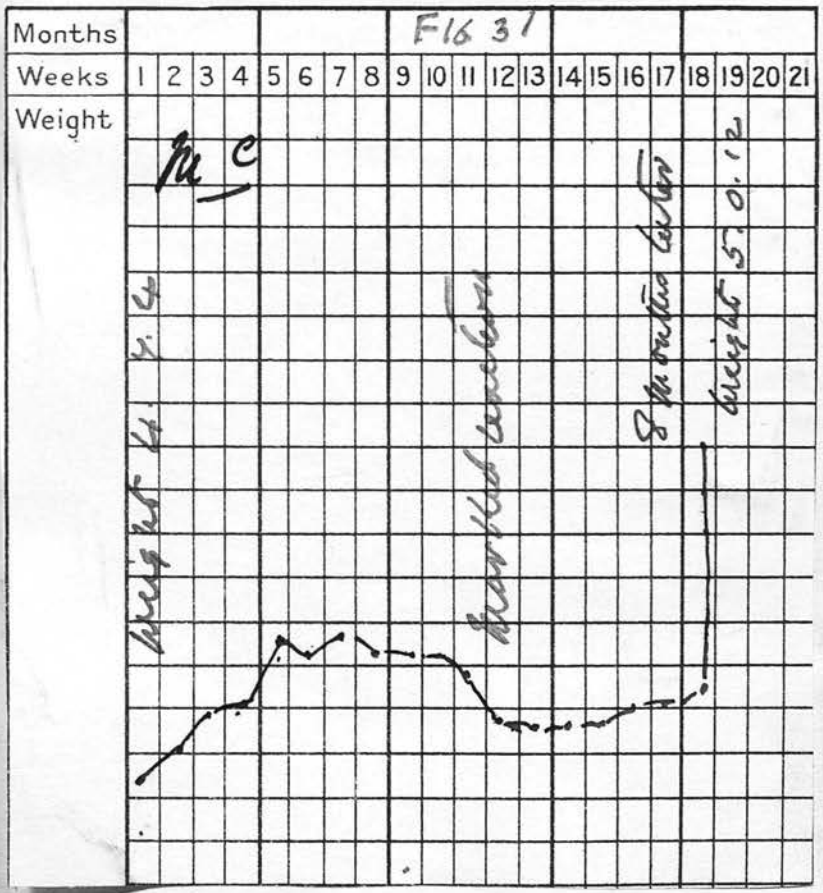
Physical Signs: Enlarged glands neak. Increased vocal resonance right apex. B.P. 100. p. 80. Hb 70. Clots in 6 minutes.

Reacted to O.T. 0005 to 100. Local reaction.

Commenced treatment with P.T.O .0002, then 0003, 00035. Reacted severely to P.T.O. 00045. No reaction on repeated dose. Treated with P.T.O. up to .6. Then P.T. up to .6.

31

FIG 25.



There are no special features about this case. The boy at one time lost a little weight, but he improved in general health very much and, as will be seen from chart, 8 months after discontinuing treatment he had gained several pounds.

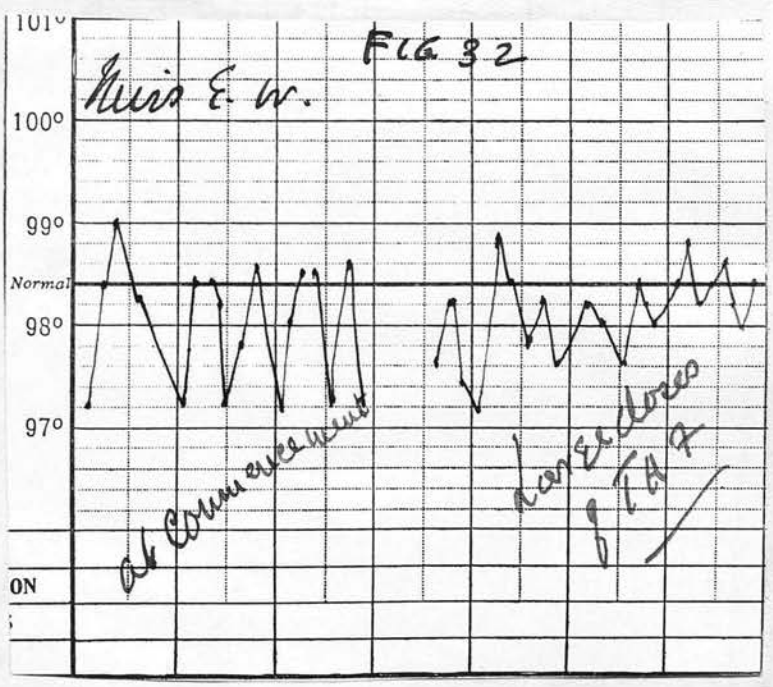
6. Miss E.W. 24. 20. 4. '20.

History: Off colour for a year. Headache daily. Biliousness. Pain after food. No vomiting. Off food. Tired. Dysmenorrhoea.

Physical signs: Loud systolic at apex, increased vocal fremitus right apex. p 90. B.P. 100. Haemoglobin 90. Clots in eight minutes.

Local reaction with O.T. 0005. Commenced treatment with P.T.O. .0005. Progressed without reactions up to P.T.O. 1 c Then treated with P.T.B. and lastly with T.A.F. up to 1.cc.

Result: On discharge was apparently well in every way. Have seen several times since and has kept in good health.



32
FIG. ~~26~~.
Miss E.W.

I made the diagnosis, and I think wisely, on the strength of the local reaction and that she felt much better. A low blood pressure, considerable difference in the morning and evening temperature, and the slight alterations in the breath sounds, decided me as to my diagnosis.

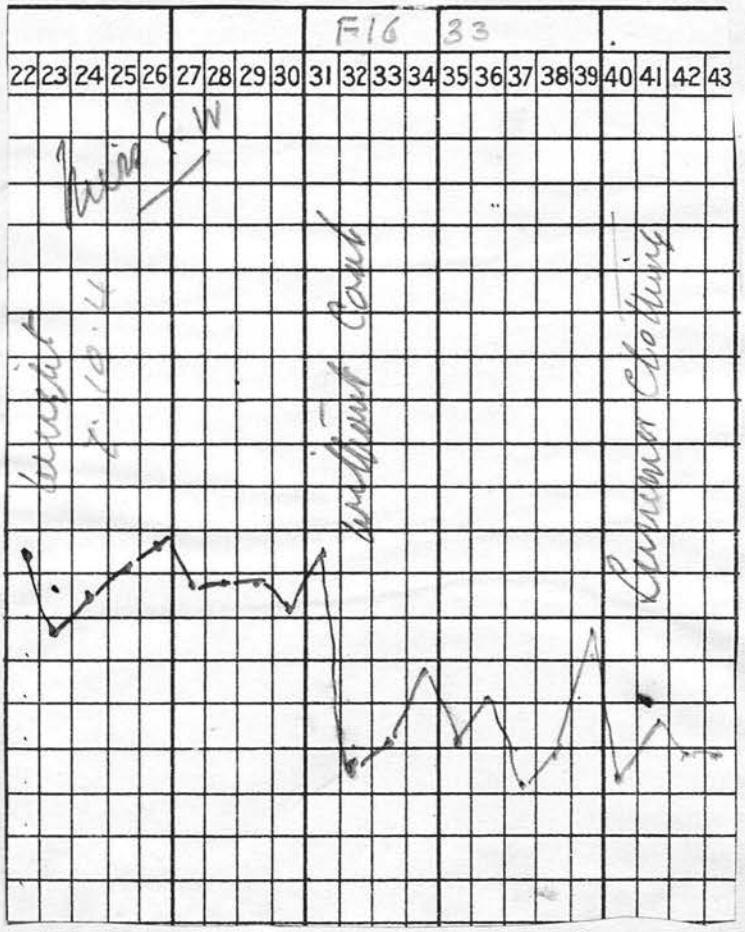


FIG. ~~34~~ 33

Miss E. W.

Note the difference in the temperature at the beginning and end of treatment.

The weight chart would give the impression of loss of weight, but it is more apparent than real and is due to seasonal changed of clothing.

7. J.S. 10 Years. 9. 7. '21.

History: 3 years ago "abscess rib" treated at Children's Hospital, Shadwell. Later developed rash, face, knees, and hands. Got worse lately. Treated at Skin Hospital without any effect.

Physical signs: Nothing to detect in the lungs. Enlarged glands neck. A chronic papular eruption, chiefly on the face. Tested with T.A.F. 0005. Reaction to 100. 2 days afterwards. This appeared to me to have no connection with the injection. I therefore repeated the dose. Reacted to 104. Felt ill; arm inflamed; eruption on face increased. Omitted treatment for 14 days. Then started on a detoxicated vaccine which produced very severe reactions till the dose was much reduced. Later took these very well. Later treated with T.A.F., commencing with .0001 which he stood remarkable well up to 1. cc.

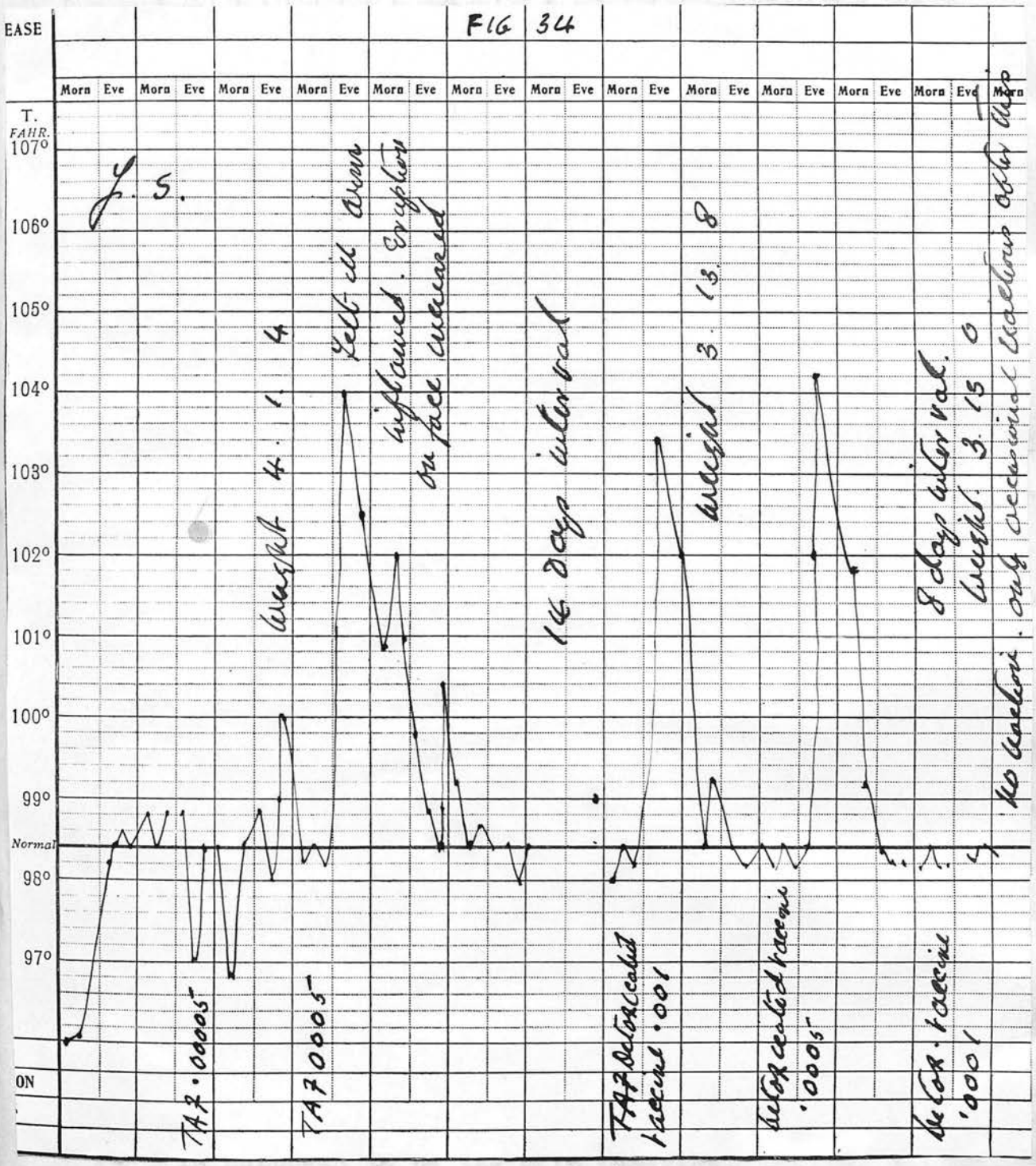
Result: He put on weight steadily and generally improved in health. After the completion of the course the eruption became much worse. I did not see him during this time, but his mother informed me that it eventually cleared and he became quite fit.

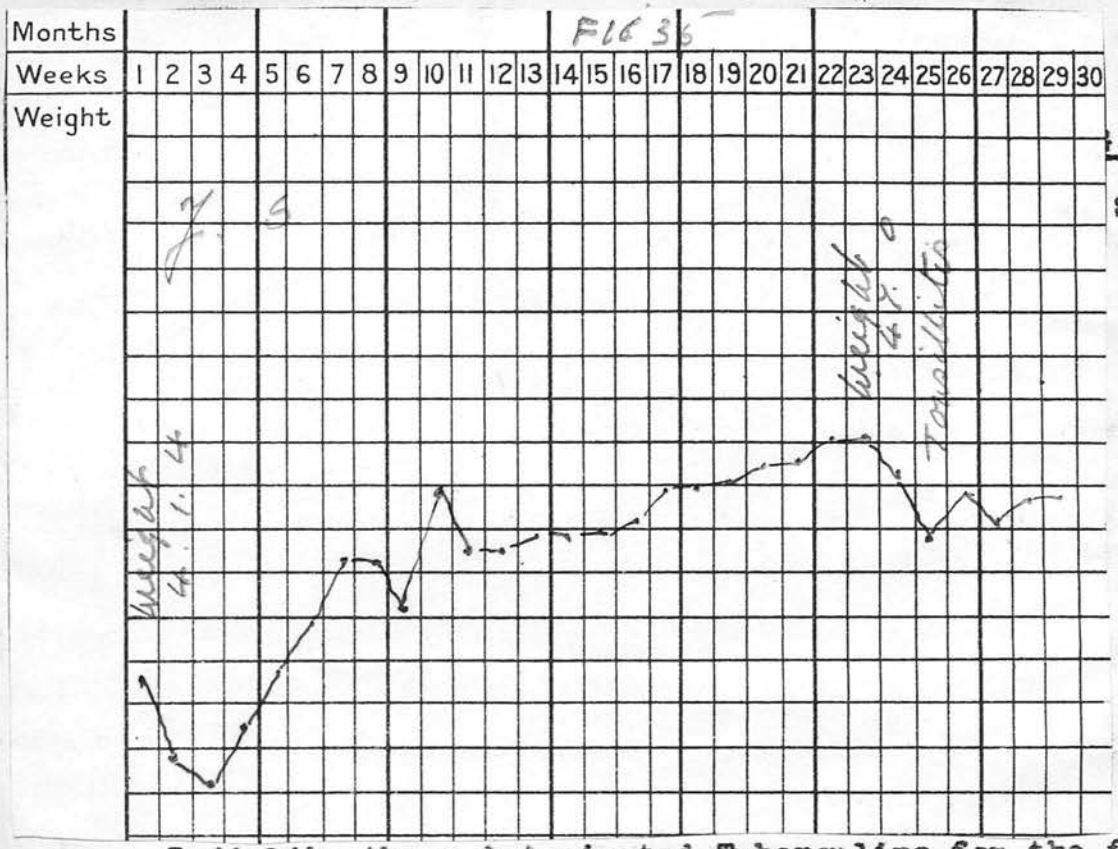
I think in this case I made a mistake in repeating the initial test dose, as the boy was a delicate little child it was probable that he would react.

It will be noted that detoxicated Tuberculin gave severe reactions.

FIG. 28.

J. S.


EASE
FIG 34
Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn Eve Morn
T.
FAHR.
107°
106°
105°
104°
103°
102°
101°
100°
99°
Normal
98°
97°
ON
J. S.
Weight 4. 1. 4
Felt ill when
unplanned. Erythem
on face increased
14 days after vacc.
Weight 3. 13. 8
8 days after vacc.
Weight 3. 15. 0
No reaction. Only occasional headache & slight
TAT 0.0005 c
TAT 0.0005 c
TAT 0.0005 c dilution 0.001
Vaccine control dilution 0.0005 c
Vaccine dilution 0.001



I dislike these detoxicated Tuberculins for the following reasons.

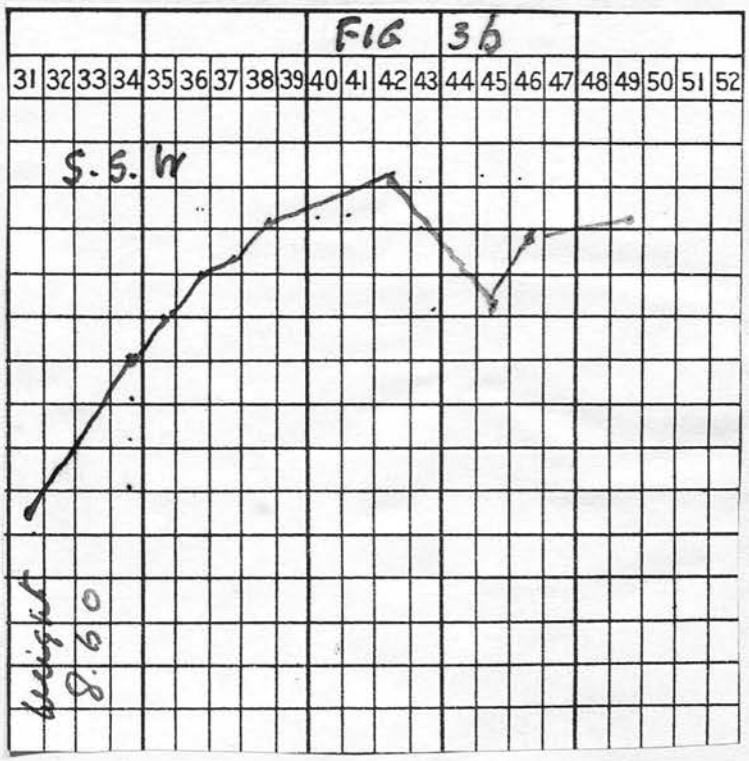
1. It means changing your preparation of Tuberculin, which, as I have previously pointed out, sometimes causes reactions.
2. I have not been able to ascertain what dose of detoxicated vaccine corresponds to a like quantity of T.A.F. so you are not sure of your dosage.
3. I have failed to see the same extent of improvement with detoxicated Tuberculin as with T.A.F. This is all the more remarkable as for detoxicated coryza vaccine I have nothing but praise.
4. Detoxication does not appear to eliminate reactions which is supposed to be its main function.

8. S.S.W. 33. Chemist. 24. 12. '20.

History: "Stomach trouble" indigestion for years. Worse when worried, better for taking pepsin. No cough. No night sweats. Stated to have had "lung trouble."

Physical examination: Stomach somewhat dilated. Liver enlarged downwards. Nothing detected in lungs. B.P. 125. p. 72. Reacted to O.T. 0005 to 100 .4. Treated with P.T.O., P.T., and T.A.F. up to 1. cc. This treatment was practically reactionless throughout and requires no detailed description.

Result: Indigestion entirely gone. Gained 6 lbs. I gave him a second course a year later and saw him at the end of 1922 apparently well.



36
FIG. 30.
S. S. W.

9. Miss E. F. 31. 29. 9. '21.

History: Constant headaches. Bowels constipated. Appetite poor. Constant colds. Night sweats.

Physical Examination: Nothing to detect in lungs or abdomen. Blood pressure 140. Hb. 80.

Reacted to 100 .8 with T.A.F. 0002; aching all over, arm painful and swollen. A week later I repeated the dose as I felt that with a blood pressure of 140 her resistance would be good. No reaction, and continued with practically no reaction till T.A.F. 1. cc.

Result: Very much better. Breathlessness gone. Appetite much better, gained 4 lbs. As she had still a cold I gave her catarrhal vaccine, which cleared this up.

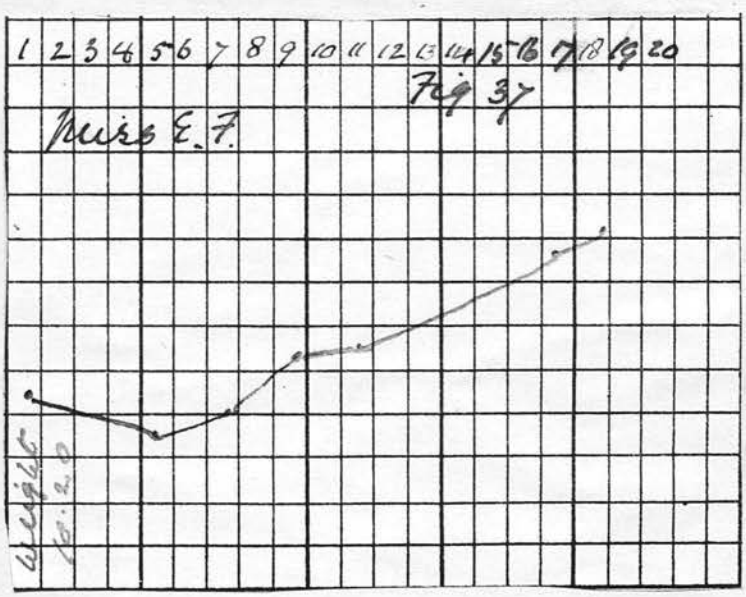


FIG. 37.

Miss E. F.

10. Mrs P. 35 years. 21. 4. '21.

History: Child born dead some years ago. 2 dilatations ovariotomy frequency of Micturition. Used to have cough. Father phthisical. Feels slack. Vomits at monthly periods and has great pain then.

Physical examination: Lungs apparently normal. Large mass of glands in right iliac fossa. B.P. 140. p. 90. Reacted to O.T. 00005 to 100. After an interval of 10 days started with P.T.O. 0002, which gave marked reaction. I reduced the dose to P.T.O. 00001, but she still reacted. I then put her on small doses of a detoxicated vaccine which she took well and I was eventually able to get her on to T.A.F. which she took without reactions up to 1. cc.

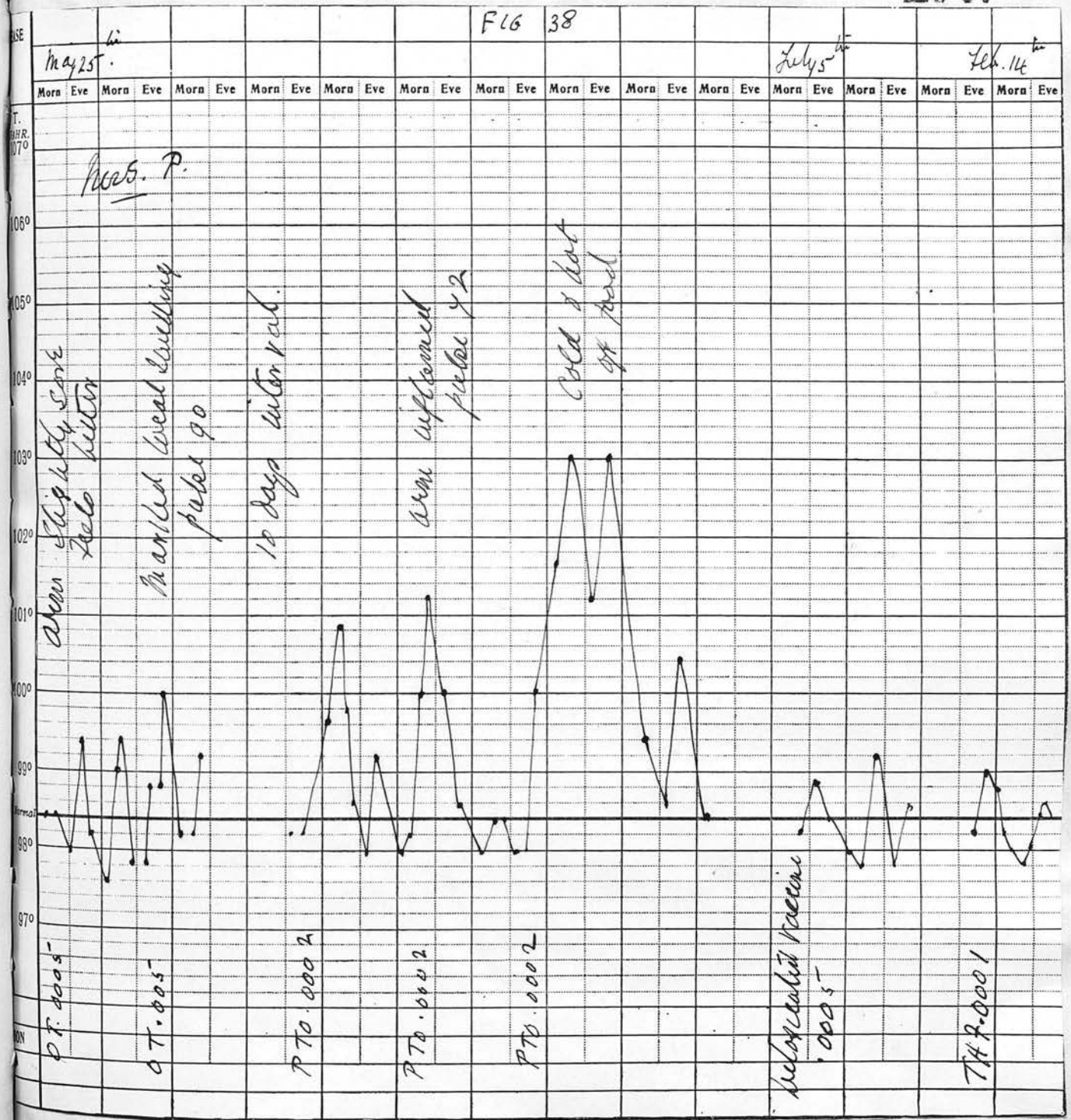
Result: The course was a very long one, but at the end of it she stated that she was much better in every way. The glands were still large, but she had more energy. The bladder trouble ceased, and there was less pain at periods.

This was a case of very marked hypersensitiveness so often seen in gland cases. Were I treating now, I should not test at all, but get on to very small, gradually increasing, doses of T.A.F. She stood the reactions well, but they are, of course, undesirable.

38

FIG. ~~32.~~

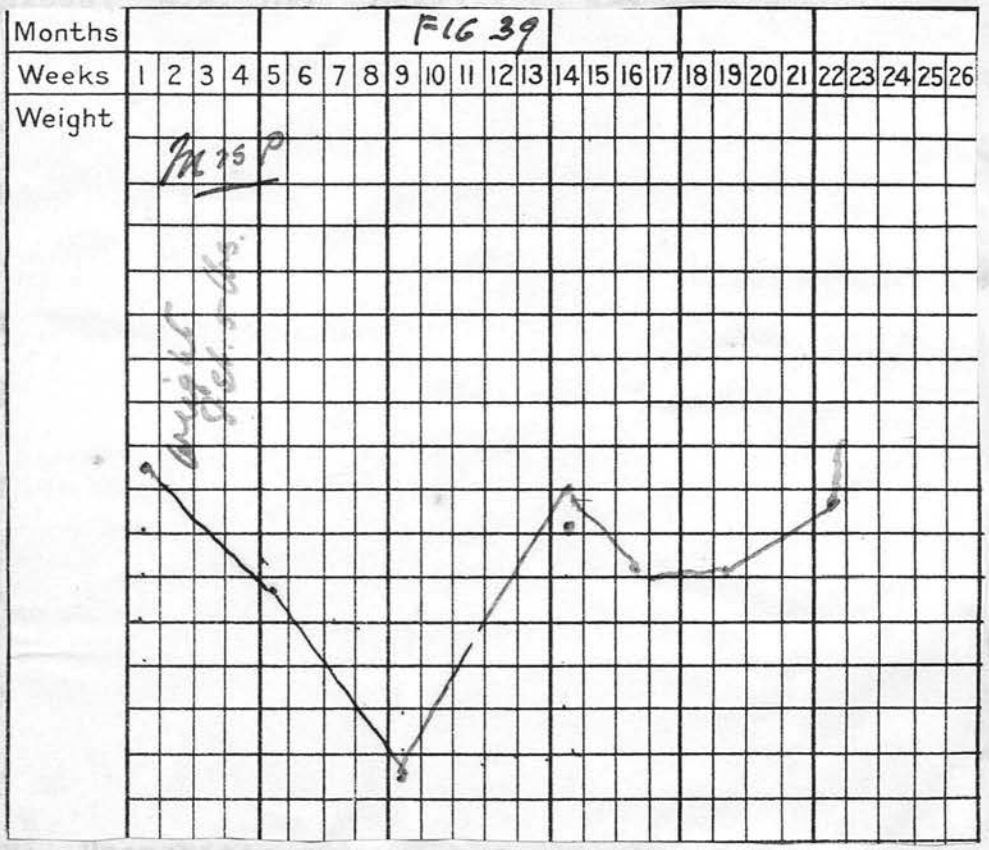
Mrs P.



59

FIG. 38.

Mrs P.



11. Mrs H. 33. 13. 7. '21.

History: 3 years duration attended Heart Hospital. Pain left side. "Stomach acid." Had rheumatism, never rheumatic fever. No cough. Lost weight. Headaches.

Physical Examination: Heart apparently normal. Friction both apices. B.P. 100. Reacted to 101 with T.A.F. 0005. After seven days gave .00005 of detoxicated vaccine. Reacted to 104. Arm very painful and swollen. Reduced to 00001. Took this and subsequent doses up to 008 well. Then put on T.A.F. 0001, which she took without reaction and was treated up to 1.cc. T.A.F.

Result: Discharged well. Gained 9 lbs in weight.

Vide Figures 2. and 15.

The error in this case was in using a detoxicated vaccine. It would have been wiser to have dropped back to small doses of T.A.F.

12. T. S. R. 26 years. 8. 11. '20.

History: Bronchitis and cough in morning for 2 years. "Slack" at end of day. Pains in stomach.

Physical examination: Rhonchi all over chest, back and front. B.P. 100. p. 90. H.b. 80. Coagulation time 6 minutes. Reacted to O.T. 0005 to 100. Arm swollen. Spat up a little blood. After a week's interval, gave P.T.O. 000 .5. Then reduced to P.T.O. 0001 for three doses. No reaction and

gradually increased up to P.T.O .5. Then treated with T.A.F. commencing with .001. He took this without reactions up to 1.cc.

Result: His weight remained about the same, but he stated at the end of the course he felt a different man. There were no abnormal physical signs to be detected in his chest.

His temperature and weight charts are of no special interest so they are not recorded here.

It will be noticed that I soon switched off from P.T.O. on to T.A.F. for at this period I was beginning to realise the virtues of the latter preparation.

13. W. F. V. 24. 19. 4. '21.

History: Began 18 months ago: followed demobilization. Pain in stomach after meals, "Waterbrash" cough, doesn't sweat. Suffers from rheumatism. "Tired."

Physical examination: Increased vocal resonance right base. Glands in neck enlarged. Liver enlarged downwards. B.P. 120. p. 72. Reacted to 100 to O.T. 0005. With the dose repeated giddy; arm swelled. Lost 3 lbs as result of reaction. Waited one week then tried with T.A.F. 0001 reacted to 105 Arm swelled; stomach swelled, but felt well. After a week gave P.T.O .00001 reacted to 103. Reduced to P.T.O. 000005, which he stood well and from this point he took doses well. After this I put him on a detoxicated vaccine which I took up

to 1. cc and then switched on to T.A.F. 001, and completed up to 1. cc without further reactions.

Result: Discharged well. Nothing to detect in lungs or liver. Gained 3 lbs.

This case brings out the folly of repeating a test dose in order to produce a classical reaction.

It also well illustrated the mistake of changing a preparation. The result of treatment was excellent, but it could easily have been obtained without such severe reactions.

FIG. 34.

W. F. V.

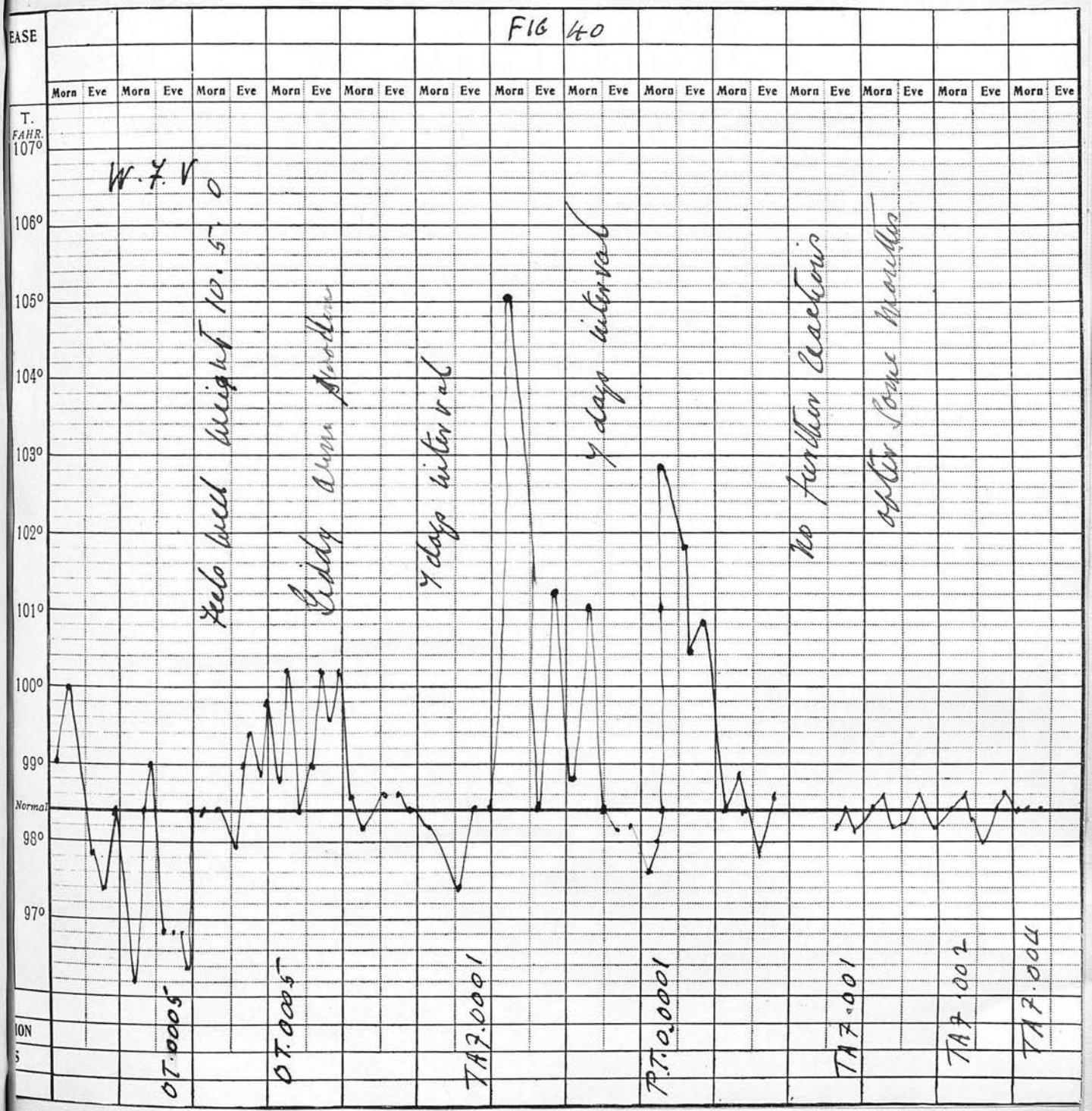


chart.

For Weight Chart see FIG. 20.

14. A. B. Aged 13 years. 11. 1. '21.

History: Since birth cough, yellow expectoration. lost weight.

Physical examination: Enlarged glands in neck, Râles ~~rhonchi~~ both lungs posteriorly. Liver enlarged. Tongue dirty. B.P. 90. Pulse 72. Hb 75. Clots in 7½ minutes. Reacted to 0004 to 100°. Arm swollen. Ten days later gave P.T.O. 0005 reacted to 101. Repeated dose, reacted to 100. Gave third time, no reaction. Then cautiously increased dosage without marked reactions, up to .6 Then went on to T.A.F. 0005, and rapidly increased up to T.A.F. .0035.

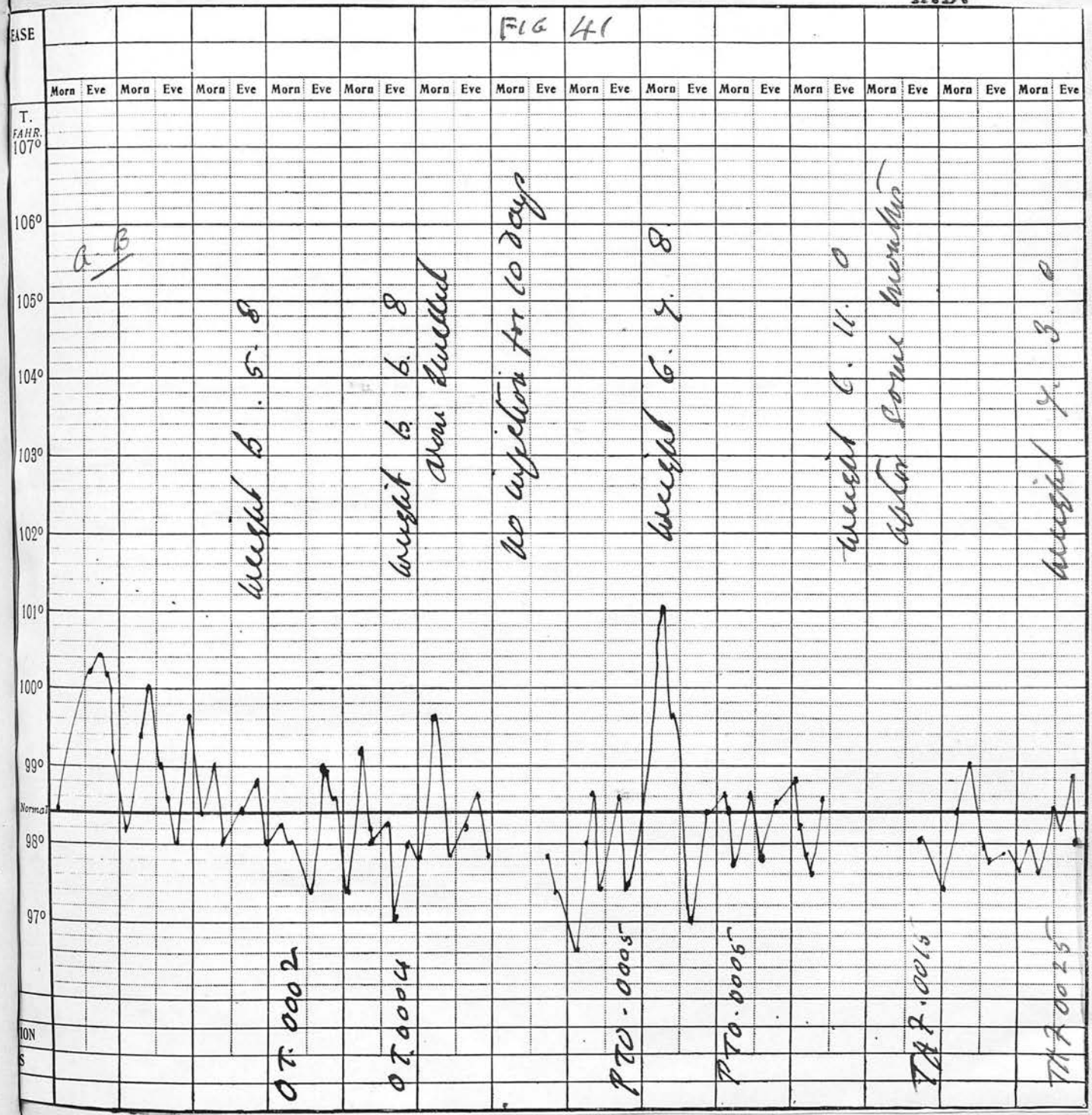
Result: Very much improved. Gained 11 pounds.

(fig 35.)

41

FIG. 35.

A.B.



This boy did remarkably well. It will be noticed how he gained in weight in spite of reactions. But this is no argument in favour of reactions.

15. Miss E.G. 24. 10. 2. '22.

History: Sleeps badly. Indigestion. Feels sick. Not lost weight. Cough three or four years. Night sweats. Pains legs, knees and shoulders. Amenorrhoea. Headaches, "tired" "off fats.

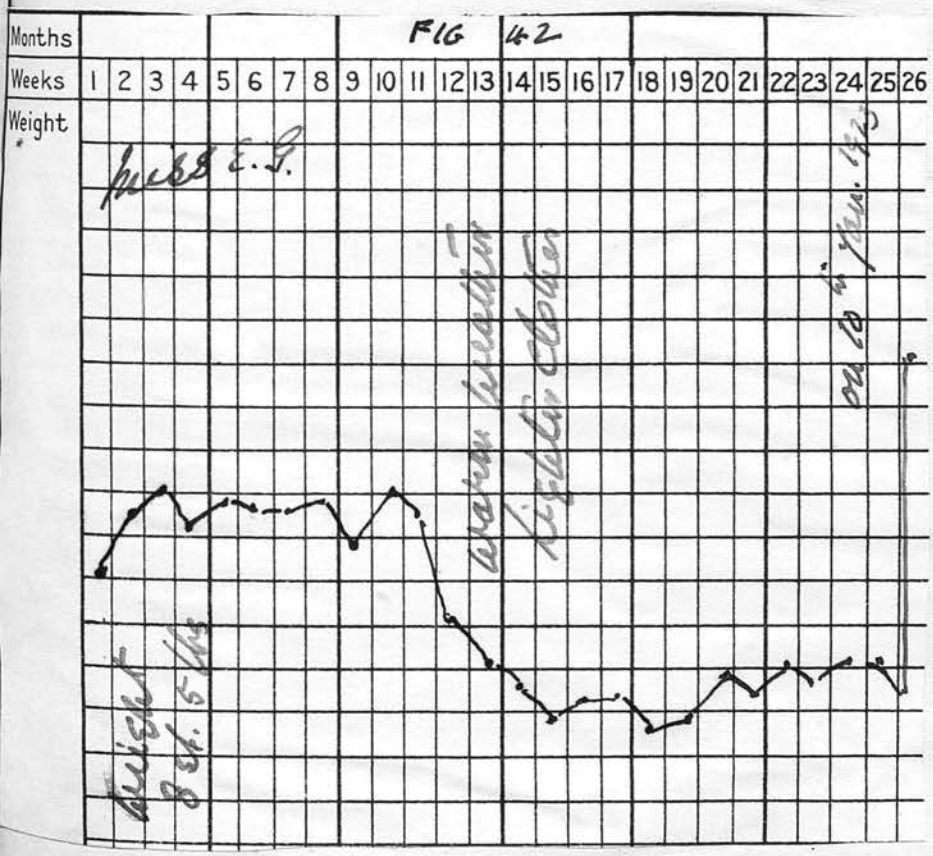
Physical examination: Enlarged glands neck. Right apex harsh breathing. Stomach dilated. Liver enlarged downwards. B.P.125. Hb 75% Clots badly. ρ 80. Reacted to T.A.F 001 to 100. Marked local reaction. Gained weight. Treated with T.A.F. commencing with .00005 up to T.A.F. 1.cc, with hardly any reactions.

Result: Lost weight, but felt better in every way.

For temperature chart see Fig. 12.

42.

FIG. 36.



It will be noticed that there is a considerable drop in weight at one period, but as she felt very well and there were no reactions, I am inclined to think that it was probably due to a very hot spell of weather.

Cases Reacting to 001

1. Mrs M. 34 years. 5. 3. '21.

History: Colds in head. Pleurisy 2 years ago. Lost weight since scarlet fever five years ago. Neurasthenic.

Physical examination: Very thin. Only one inch expansion of chest, otherwise no definite physical signs. B.P. 96. p. 80. Hb. 65. Coagulation time 6 minutes.

Reacted to 100 with O.T. 001. Local reaction. After a week put on P.T.O, commencing with P.T.O. 0005. I was able to rapidly increase the doses as she had no reactions. She had P.T.O up to .6 Then T.A.B, commencing with .06 up to 1. cc.

Result: Very great improvement. She stated she felt 20 years younger, and she was much less nervous. Gained 5¾ lbs in weight.

The temperature chart is of no special interest so it is not shewn.

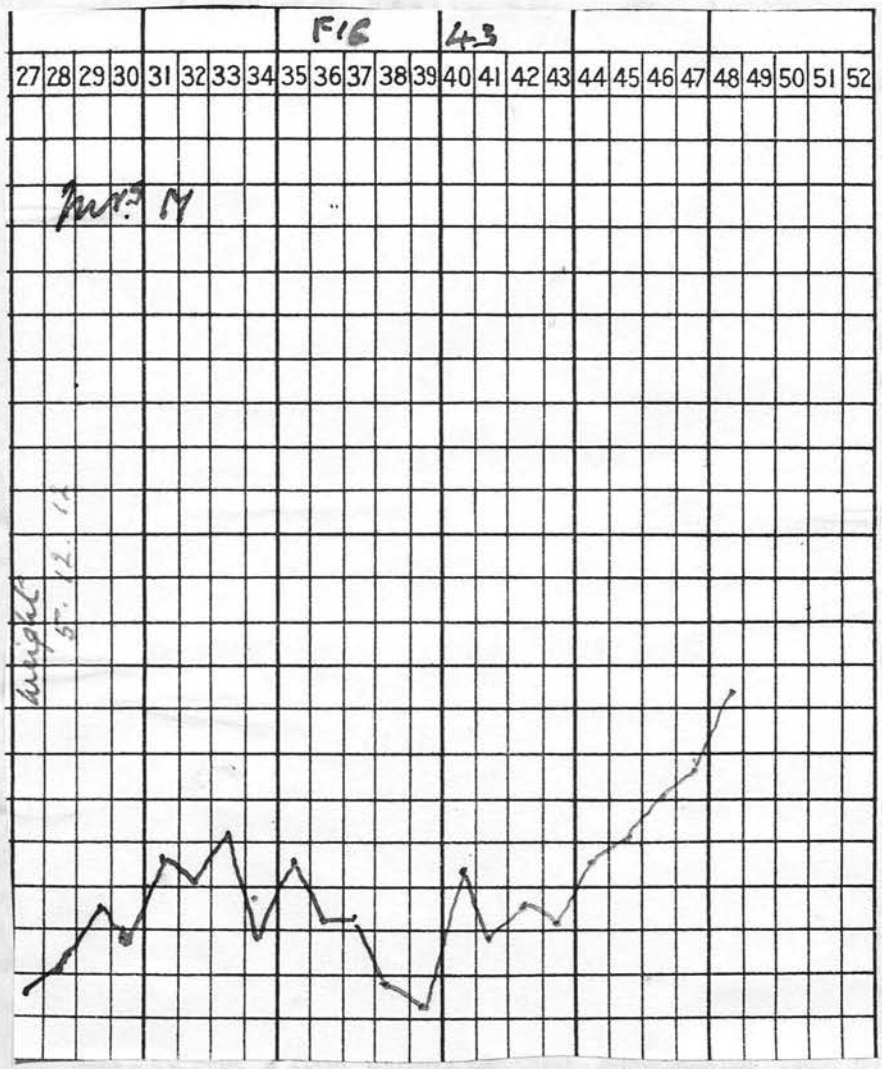
Weight chart attached.

43

FIG. ~~37.~~

Mrs M.

Weight Chart.



2. J. M. Aged 6. Son of Mrs M.

A peevish little boy. Glands in neck enlarged. Nothing to detect in lungs. Reacted to 102 with O.T. 002. Local reaction and cough.

After ten days interval gave P.T.O. .001; no reaction. Had marked reactions whilst taking small doses of P.T.O., but later quieted down. Treated with P.T.O. up to 1. cc. Then P.T. up to .6 followed by T.A.F. up to 1. cc. T.A.F. suited him much best.

Result: Though he did not gain weight, he became much less irritable and he appeared better in every way. Later he had his tonsils removed at Great Ormond Street, which improved his health a good deal.

Attached are part of temperature chart, and weight chart, of this boy.

It will be noticed that there was no appreciable gain in weight, which is unusual. Possibly the fact that he was suffering from tonsils and adenoids may account for this.

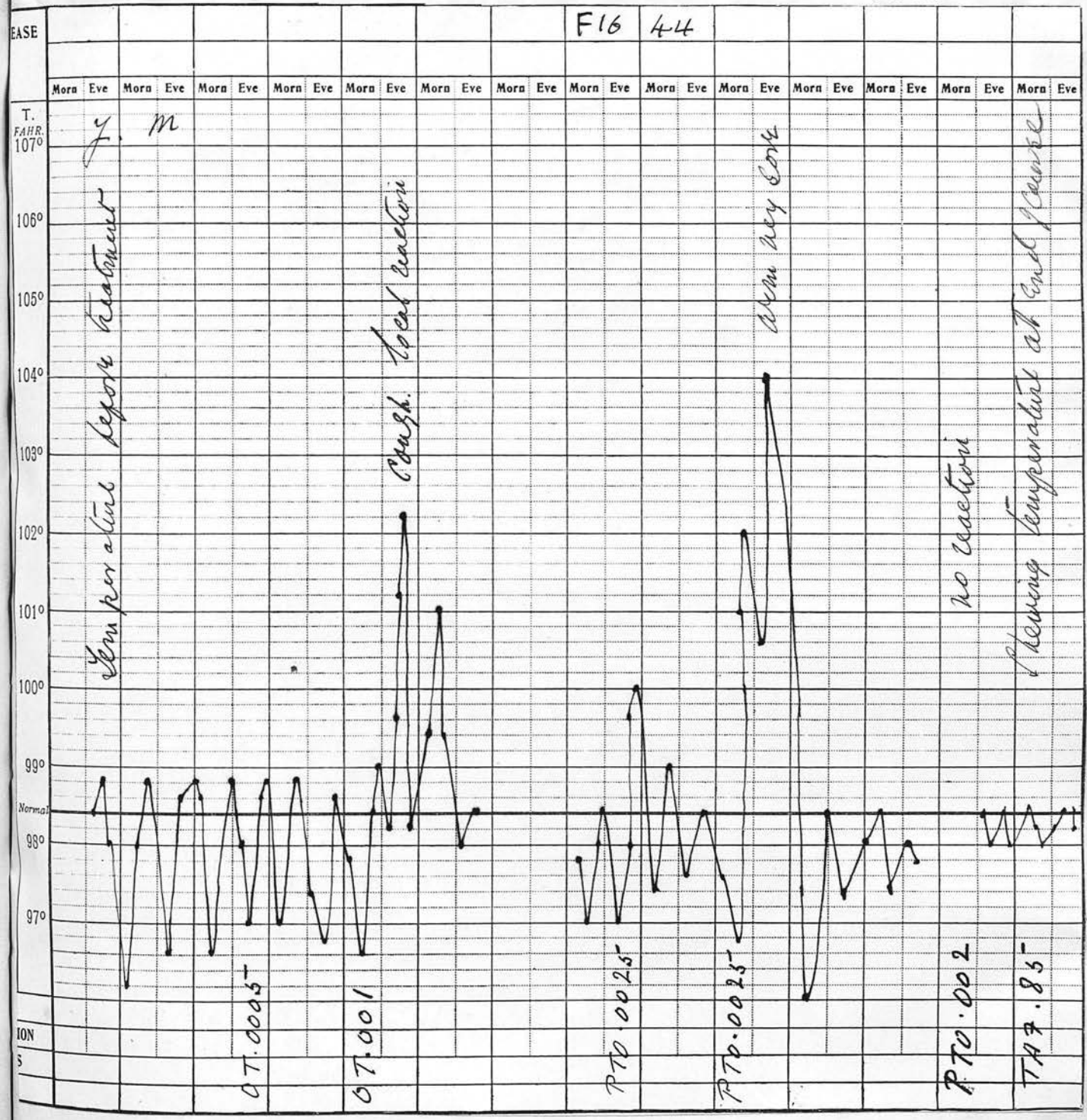
It will be seen that he had severe reactions, but they did not affect his health, in fact he appeared better.

Note severe reaction on repetition of same dose of P.T.O. 0025. No reaction when dose was slightly reduced.

Also note the even morning and evening temperature at end of course, and contrast with that before treatment.

FIG. 38.

J. M.



Temperature Chart.

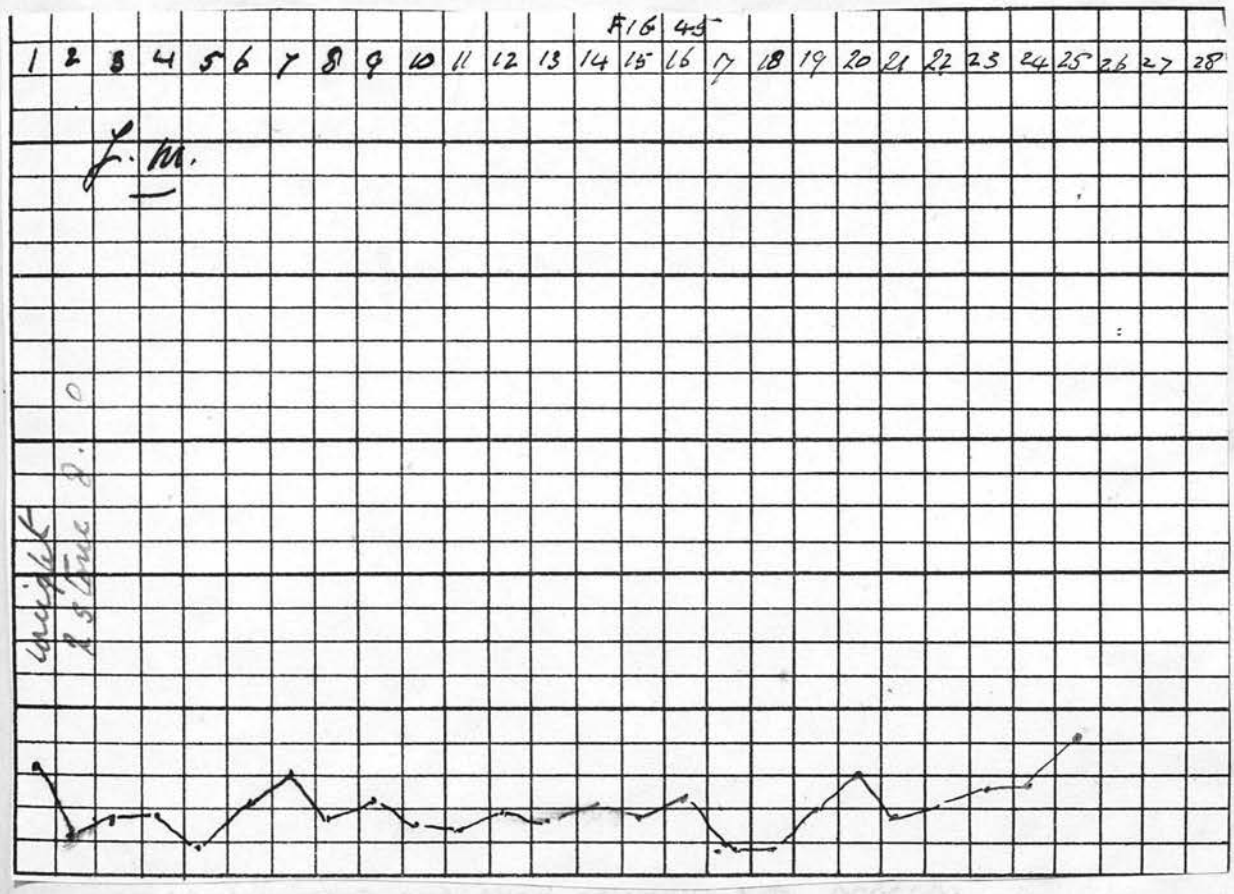


FIG. 39. 45

J. M. Weight Chart.

3. V. S. 12 years. 1. 8. '21.

History: Tired; irritable for some time. Glands in neck enlarged. Hb, 80. B.P. 90. Nothing to detect in lungs.

Reacted to 99 with T.A.F. 001. Four days later reacted to 105 with T.A.F. 00005. Feels well, but cold. Marked local reaction. Waited seven days then gave T.A.F. 000005; reacted to 103. A week later gave P.T.O. 00001 reacted to 102 .8.

In spite of severe reactions gained 3 lbs in weight. Then put on small doses of detoxicated vaccine, which did not cause reactions. Treated her with this up to .004 Then put her on T.A.F. 0005, and treated her without any more reactions up to T.A.F. 1. cc.

Result: Absolutely well. Gained 1 st. 2 lbs in weight.

The error in this case was in giving a dose so quickly after initial reaction. It would have been better to have waited a week and then given T.A.F. 0000001.

46

FIG. 40.

V. S.

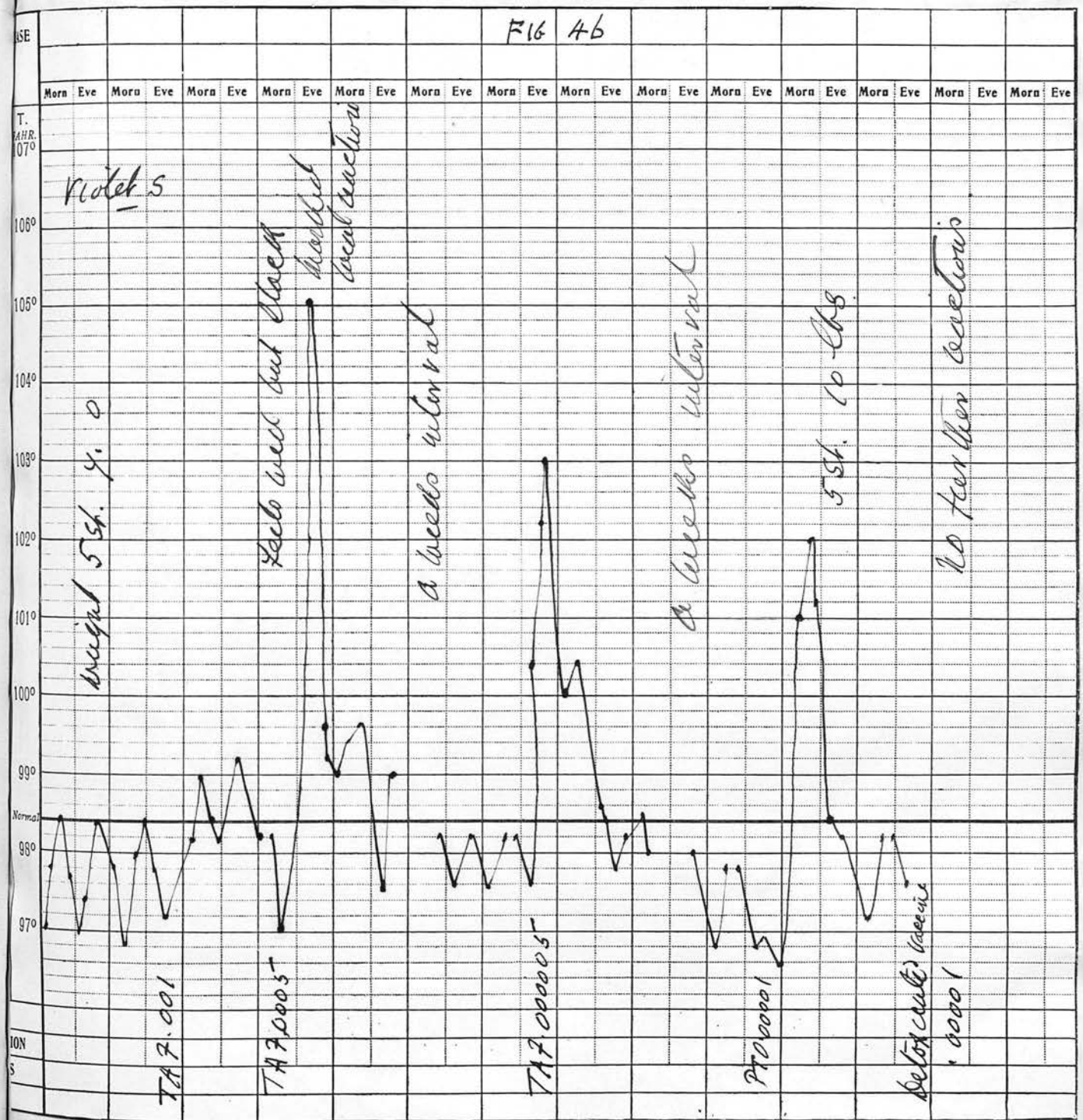
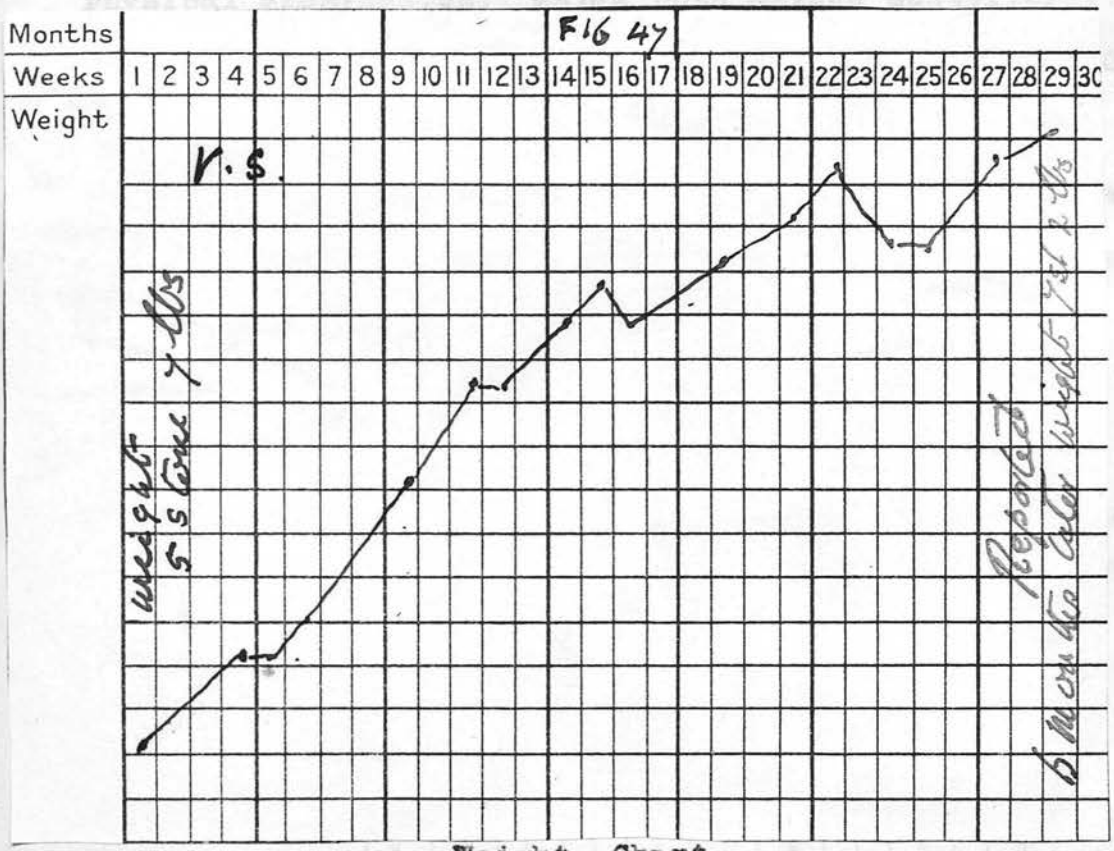


FIG 46
Morn Eve
T. 107°
106°
105°
104°
103°
102°
101°
100°
99°
Normal
98°
97°
Violet 5
weight 5 Sk. 4. 0
Had used but Week
Moderate
Convulsions
a weeks interval
a weeks interval
5 Sk. 10 Cms.
10 Hourly Convulsions
TA 7.001
TA 7.0003+
TA 7.000005+
PD 00001
Delirium (absence
1.0001

FIG. 41.

V. S.



Weight Chart.

4. Mrs S. 33. 16. 5. '20.

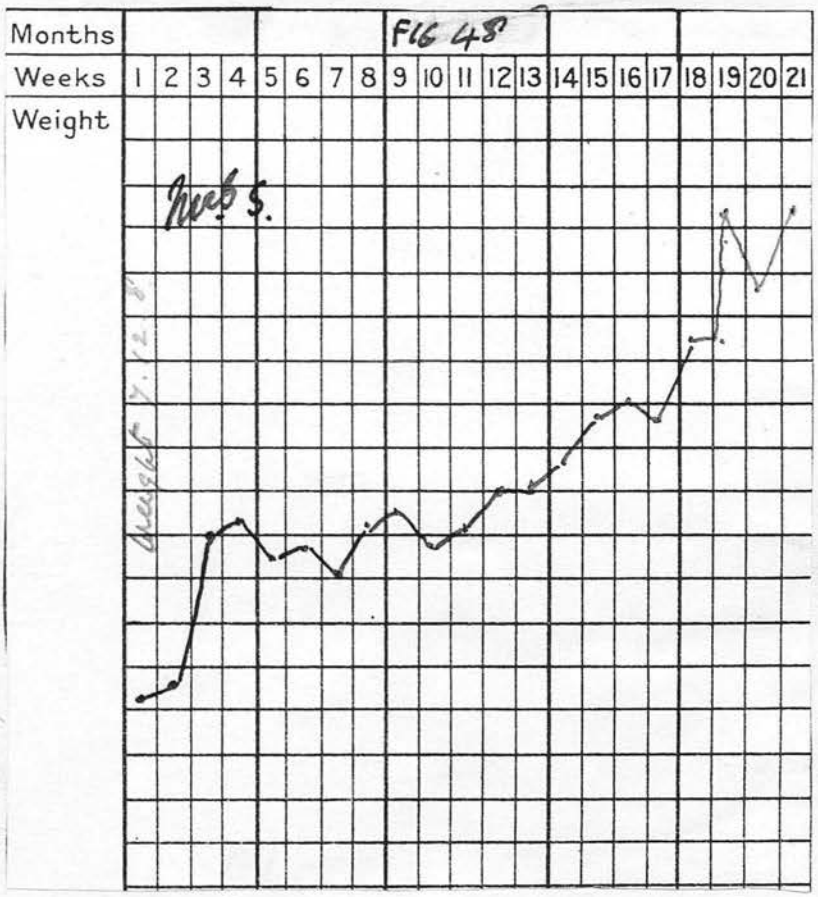
History: Cough for some years. Father and brother consumptive.

Physical examination: Rales both apices posteriorly.

Reacted to O.T. 001. Treated with P.T.O. P.T. and O.T. up to 1. cc without further reactions.

Result: Very much better. Gained nearly 10 lbs in weight.

The case calls for no special remarks. It was a perfectly straightforward one.

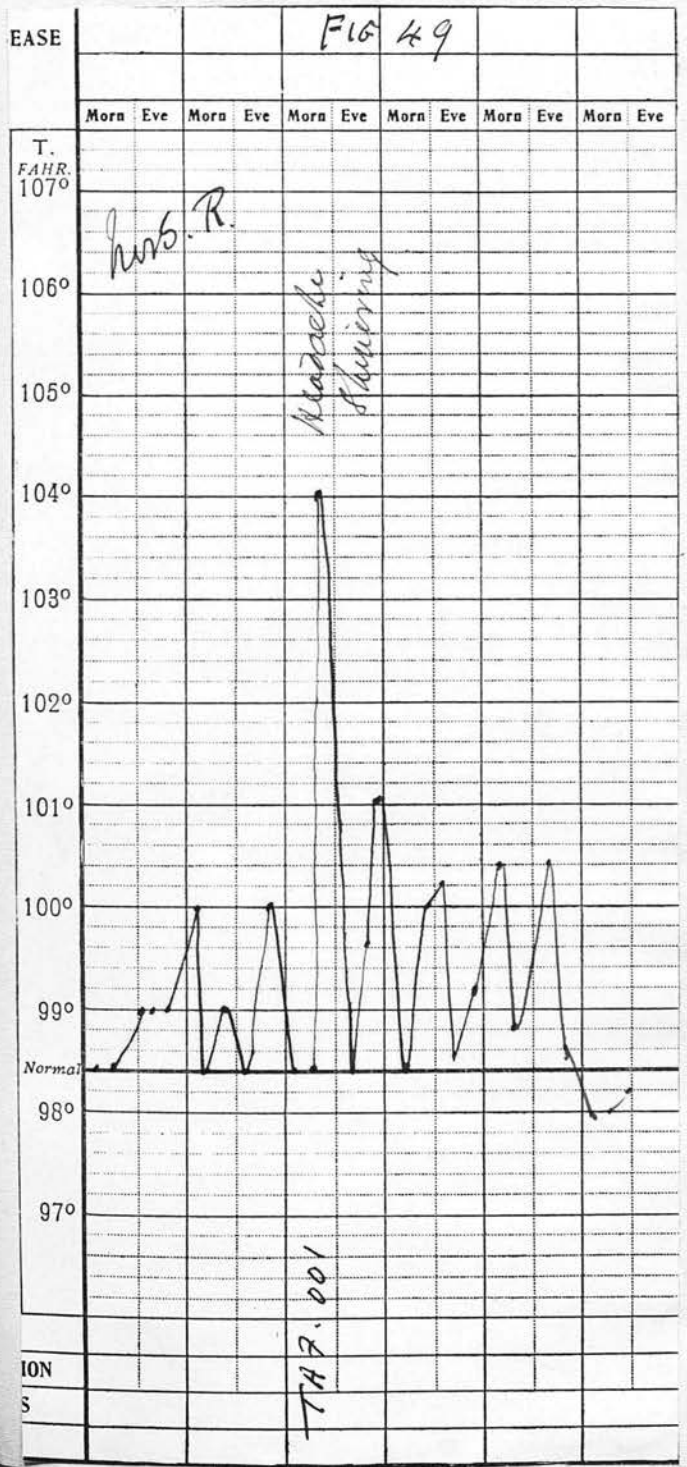


Weight Chart. Mrs S.

5. Mrs R. 44 years. 15. 8. '21.

History: Operated on for septic peritonitis following a miscarriage last November. Bad health for years. Languid, sleepy, easily exhausted, catches cold easily. Lost 3 st. since operation. Bad family history.

FIG. ~~43~~ 49. (Mrs R.)



Physical examination: Teeth very bad. Stomach dilated. Lungs and heart apparently normal. B.P. 100. Very nervous. Von Pirquet's reaction negative. She reacted sharply to T.A.F. 001 to 104., vide chart.

I did not treat her. It is a class of case who really should not be tested, and if treated at all should be dealt with very cautiously on account of the neurotic condition.

6. Miss E. C. 20. 31. 1. '21.

History: Influenza two years ago. Cold sweats night and day. Very tired. No cough. Good appetite. Irritable.

Physical examination: "Tremors." Dirty tongue. Glands in neck enlarged. Liver enlarged. Lungs normal. B.P. 90. Reacted to 99 . 4 with marked local reaction with O.T. .001 Reacted very severely with small doses of P.T.O. up to .0005. The treatment did her no good. She lost several pounds in weight and it was discontinued. Possibly she might have done better on T.A.F.

7. E.C. 29. 21. 4. '21. Attending West End Hospital for Epilepsy.

History of Epilepsy "slack" Cough.

Physical examination: Harsh breathing. Left apex - X ray revealed a small suspicious shadow at left apex.

Reacted to 102 with O.T. .001 Giddy, "falling down feeling" Vomited. Treated with T.A.F. commencing with .0001 and completed a practically reactionless course up to T.A.F. 1. cc.

Result: Lost 4 lbs, but had no fits after early in the treatment. Stated he felt infinitely better, with more energy. Saw a year later apparently well.

The interest in this case is the effect the Tuberculin had on the epilepsy.

8. Mrs B. 54. 2. 11. '20.

History: "Run down" for a month or so. Depressed. Cough in morning. Effort to get up. Had a hemorrhage from an old gastric ulcer. Night sweats. Mother died of phthisis.

Physical examination: Nothing to detect in lungs. B.P. 140. Hb. 90% Reacted to 102 with O.T. 001. Treated with P.T.O. P.T. and O.T. up to 1. cc. Treatment was reactionless practically and there was no change in weight.

Result: Said at the end she was better than she had felt for years. Saw again a year later, quite well.

9. Miss W.A. 23. 18. 4. '21.

History: Pains in stomach and back 3 or 4 days. Often had influenza. Feels "finished". Irritable. Lost weight.

Physical examination: Expiration prolonged right apex posteriorly. Stomach dilated. B.P. 90. Haemoglobin 65. Clots in 7 minutes. Reacted to O.T. 001 to 99 .8. Treated with P.T.O. commencing with .0001 up to .015, and then with T.A.F. commencing with .0001 Completed course up to 1. cc. Practically reactionless except for first few doses.

Result: Apparently absolutely well. Gained 8 lbs in weight.

For weight chart see Fig. 19.

10. Mrs N. 28 years. 12. 2. '21.

History: Pain between shoulders 3 years. Bowels constipated chronic colds, lost weight, depressed.

Physical examination: Lungs apparently normal. Stomach dilated. B.P. 138. Hb. 70. Reacted to 99 .8 with O.T. 001 Marked local reaction. Treated with P.T.O. P.T. and T.A.F. up to 1. cc. No reactions.

Result: Lost a little weight, but was discharged absolutely well.

Gave a second course a year later as she complained of being "run down". It seemed to pull her together again, as the former course did.

11. Miss D. 20. 27. 1. '21.

History: "Lumps in neck," for some time. Tired.

Physical examination: Large gland right side of neck. Lungs apparently normal.

Reacted to O.T. 001 to 101. Began treatment with P.T.O. 0005 but this gave a severe reaction, which increased on repeating. Put back to P.T.O. 0001, but this gave reactions. Then tried a detoxicated vaccine which eventually she took without reactions, and I then got her on to T.A.F., which she stood fairly well, but I had to discontinue at T.A.F. 04 as she got continuous reactions.

Result: The gland in her neck disappeared and her general health improved, but the reactions were undoubtedly undesirably severe. Were I to treat such a case now I should begin with T.A.F. 00000001, or some such dose, and I think the results would be better.

12. Miss M. H. 35. 8. 5. '22.

Depressed. Pain left breast and left shoulder. Sweats constantly. No cough. Indigestion. Father and Mother died of phthisis.

Physical examination: Nothing to detect in lungs. Stomach dilated. B.P. 135. Blood clots well. Hb .75% Pulse 68. Reacted to T.A.F. 001 to 3rd dose to 100 .5 Commenced dosing with T.A.F. 0001 and continued with practically no reactions up to 1. cc.

Result: Discharged absolutely well. Gained 3½ lbs in weight. Her temperature chart is interesting, showing the effect of cautious testing. Reacted to 3rd repetition of same dose.

Note deleterious effect of doubling a dose.

Note also rapid gain in weight with larger doses.

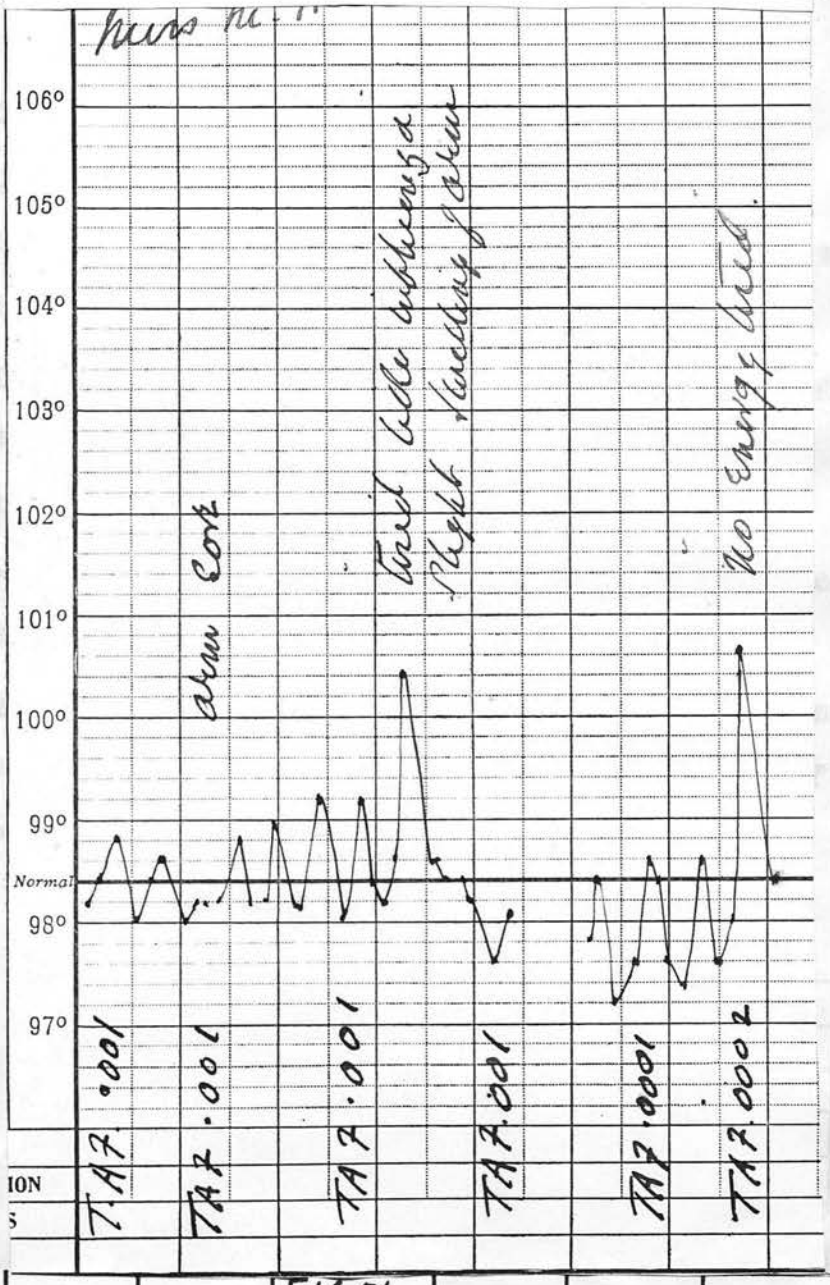


FIG. ~~44~~ 50.

Miss M. H.

Temperature chart.

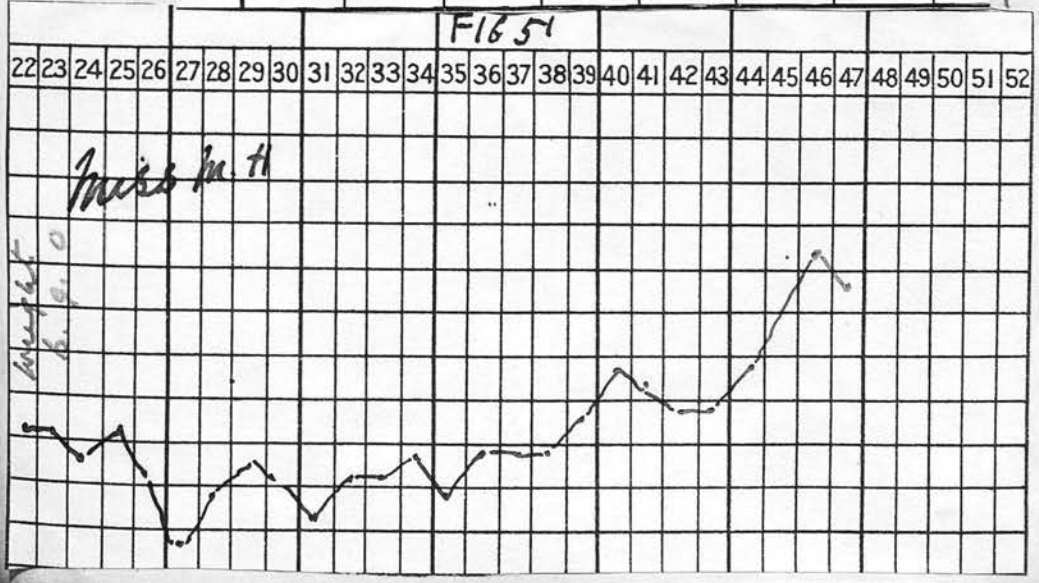


FIG. ~~45~~ 51.

Miss M. H.

Weight chart.

13. Miss W. J. 23. 15. 6. '21.

History: 8 months "no life." Depressed. Palpitation since she can remember. Night sweats. Lost weight. "Blushing" after meals.

Physical examination: Harsh breathing right apex posteriorly.

Reacted to T.A.F. 001 to 100.

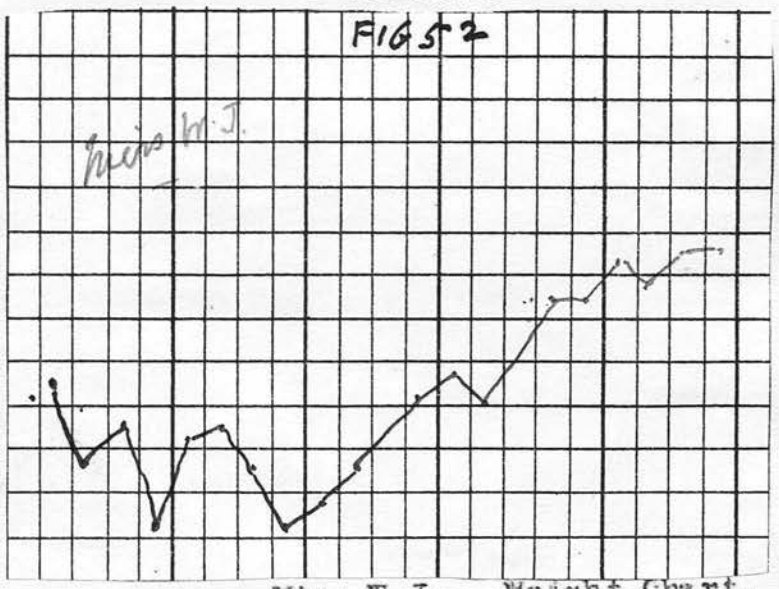
Treated with a detoxicated vaccine up to .6 Then began with T.A.F. 003 and rapidly increased up to 1. cc.

Treatment reactionless throughout.

Result: Felt absolutely well at end. Gained 3 lbs.

Saw again Jan. 23. Weight the same, but a few symptoms coming back, so giving a second course.

FIG. ~~48.~~ 52



Miss W.J. Weight Chart.

Cases Reacting to 002.

1. A.T.B. Aged 30. 19. 11. '20.

History: Cough; pain in left side for some time. Feels slack. Lost weight. Night sweats.

Physical examination: Slight friction left base. Weight 10 st. 2 lbs. Reacted to O.T. 002 to 103

Treated with P.T.O. commencing with .001. P.T. and O.T. up to 1. cc without reactions.

Result: Gained 4 lbs in weight and feels much better. Have seen him several times since and he has remained quite fit.

2. Miss H.V. 22. 24. 6. '20.

History: Cough and colds for a month. Night sweats. Yellow expectoration. Lost weight.

Physical examination: Increased V.R. right apex.

Reacted to 103 with O.T. 002 and subsequently had severe reactions with P.T.O. but eventually became desensitized.

Treated with P.T.O. P.T. and O.T. up to 1. cc.

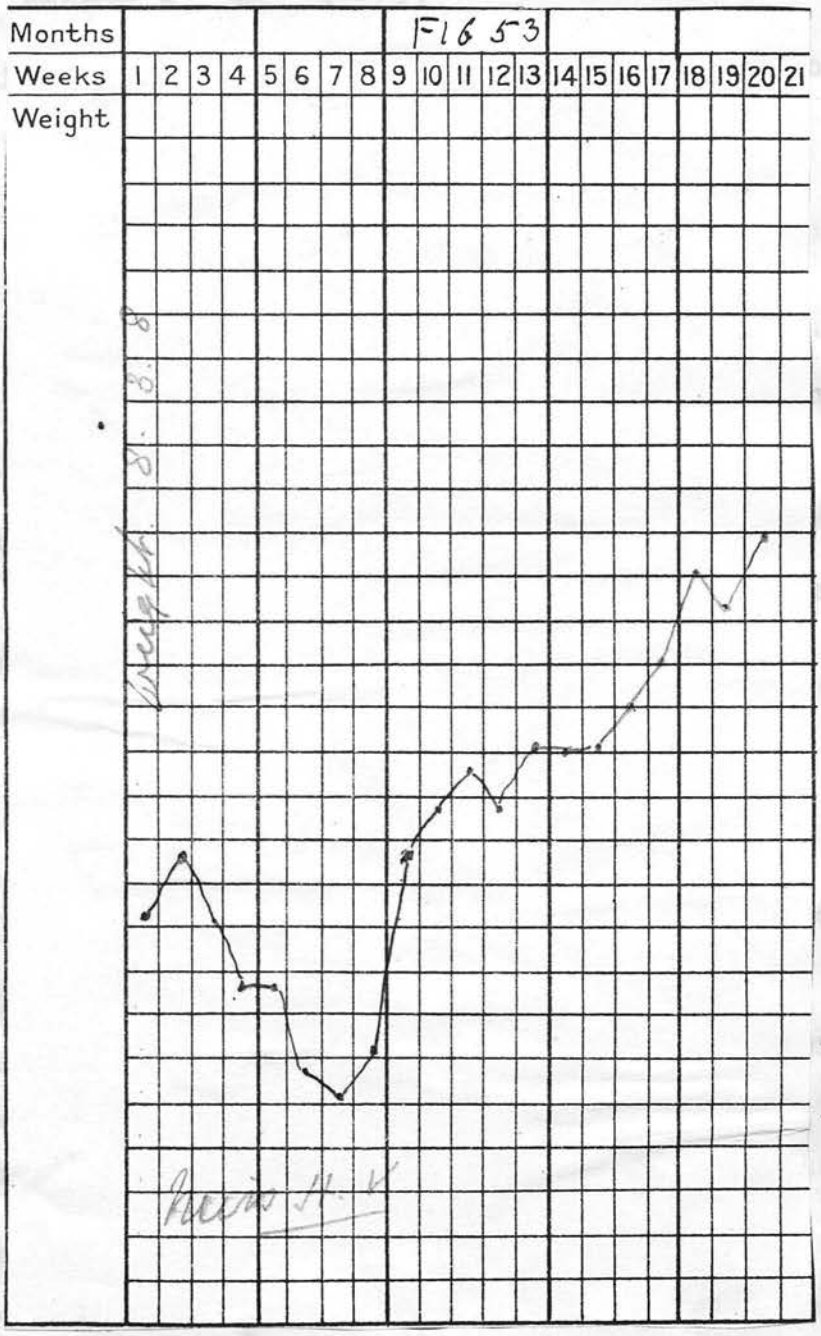
Result: Discharged absolutely well. Gained 8 lbs in weight.

See attached chart.

53

FIG. 47.

Miss H. V.



Note fall of weight at beginning during period of reactions, and steady after rise when desensitized.

3. Arthur M. 21. 3. '21.

History: Cough some time. Run down. Off food. Dental caries.

Physical examination: Enlarged glands neck. Hb. 60. Clots in 7 minutes.

Reacted to 103 with O.T. 002. Treated with P.T.O. up to .2 then T.A.F. from .001 to 1. cc with practically no reactions.

Result: Absolutely well on discharge. Gained 5 lbs in weight. Saw again 6 months later. "Absolutely different. Good at school and games, and doesn't get colds.

For weight chart see Fig. 1.

4. E.W.C. 4. 3. '21.

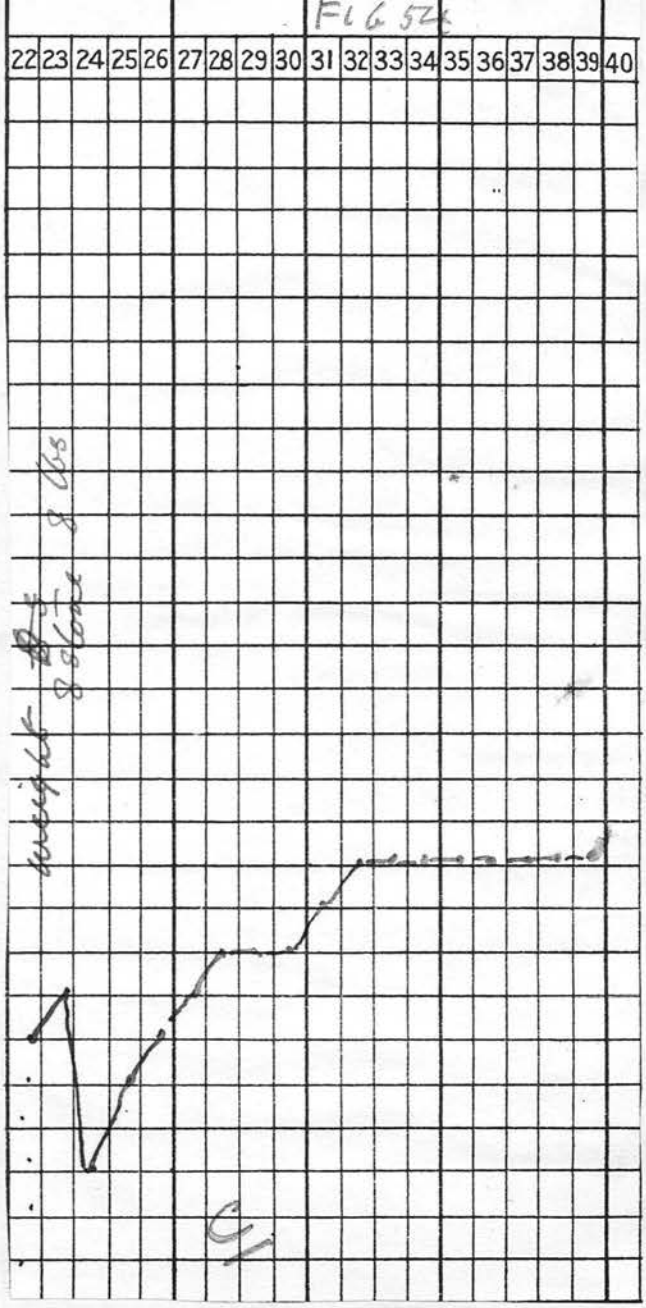
History: Twelve months previously pneumonia and pleurisy. "Loss of energy." Rheumatism.

Physical examination: Increased V.R. both apices, with harsh breathing. B.P. 110. Hb. 80. p. 90.

Reacted to O.T. 002 to 103. Headache; shivering; arm swollen. A week later commenced treatment with P.T.O. .0005 up to 1. cc then P.T. and finished with T.A.F. up to 1. cc without reactions.

Result: On discharge feels well, never any aches or pains.

See chart attached.



54

FIG. 48.

With my present knowledge am inclined to think that treatment here was unnecessarily prolonged; there was no gain in weight after P.T.O .04 was given.

5. Kathleen G. 25. 11. '20.

History: 2 years ago influenza. Since then off food. Bowels constipated. Mother, and father, and brother died of phthisis. Very tired, lost 2½ lbs weight in 3 weeks.

Physical examination: A highly nervous child. Expansion of chest poor. Harsh breathing both apices. Reacted to 002 O.T. to 100 Treated with P.T.O. P.T. and T.A.F. up to 1. cc practically reactionless.

Result: Apparently quite well. Nervousness entirely gone. Gained 2 lbs in weight. Saw 9 months later improvement continued, gained another 5 lbs in weight.

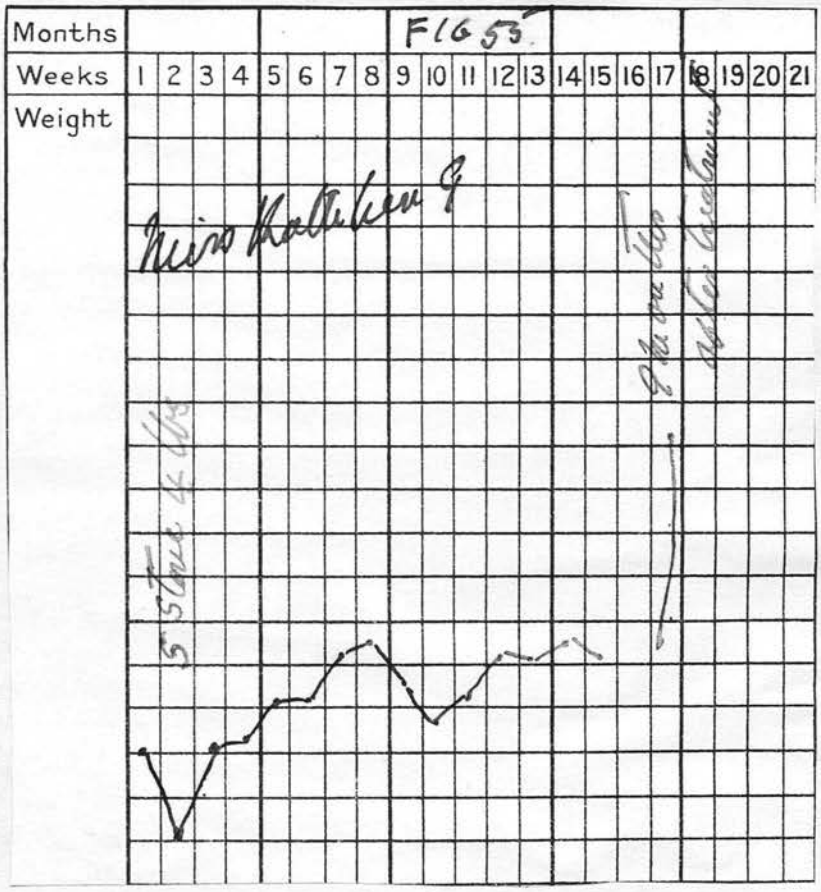


FIG. ~~49~~ 55.

6. Mrs. L. 37 years. 31. 7. '20.

History: Treated for years at Victoria Park Hospital and Homeopathic Hospital for years for "asthma".

Physical examination: Limited expansion of chest. Stomach dilated.

Reacted to O.T. 002 Marked local reaction. Temp. 101. Asthma much less.

Commenced treatment with P.T.O. 0005 and continued up to .9. Then treated with P.T. up to .08. Entirely reaction-less.

Result: Asthma very much less-ened. Gained 8 lbs in weight. She then had a bad attack of bronchitis and did not go on with the treatment.

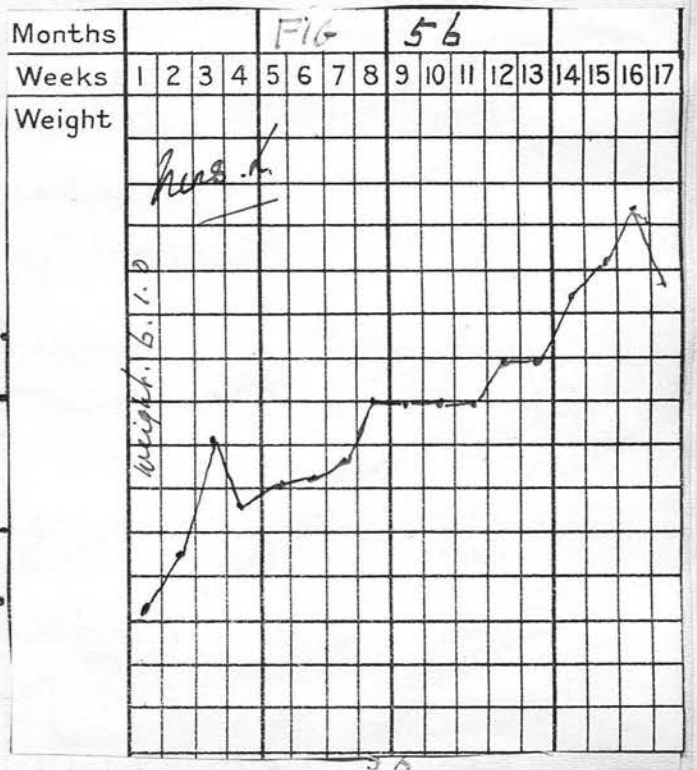


FIG. 50.

7. Miss A.H. 32. 25. 2. '26.

History: Colds every winter. Cough. Expectoration. Night sweats.

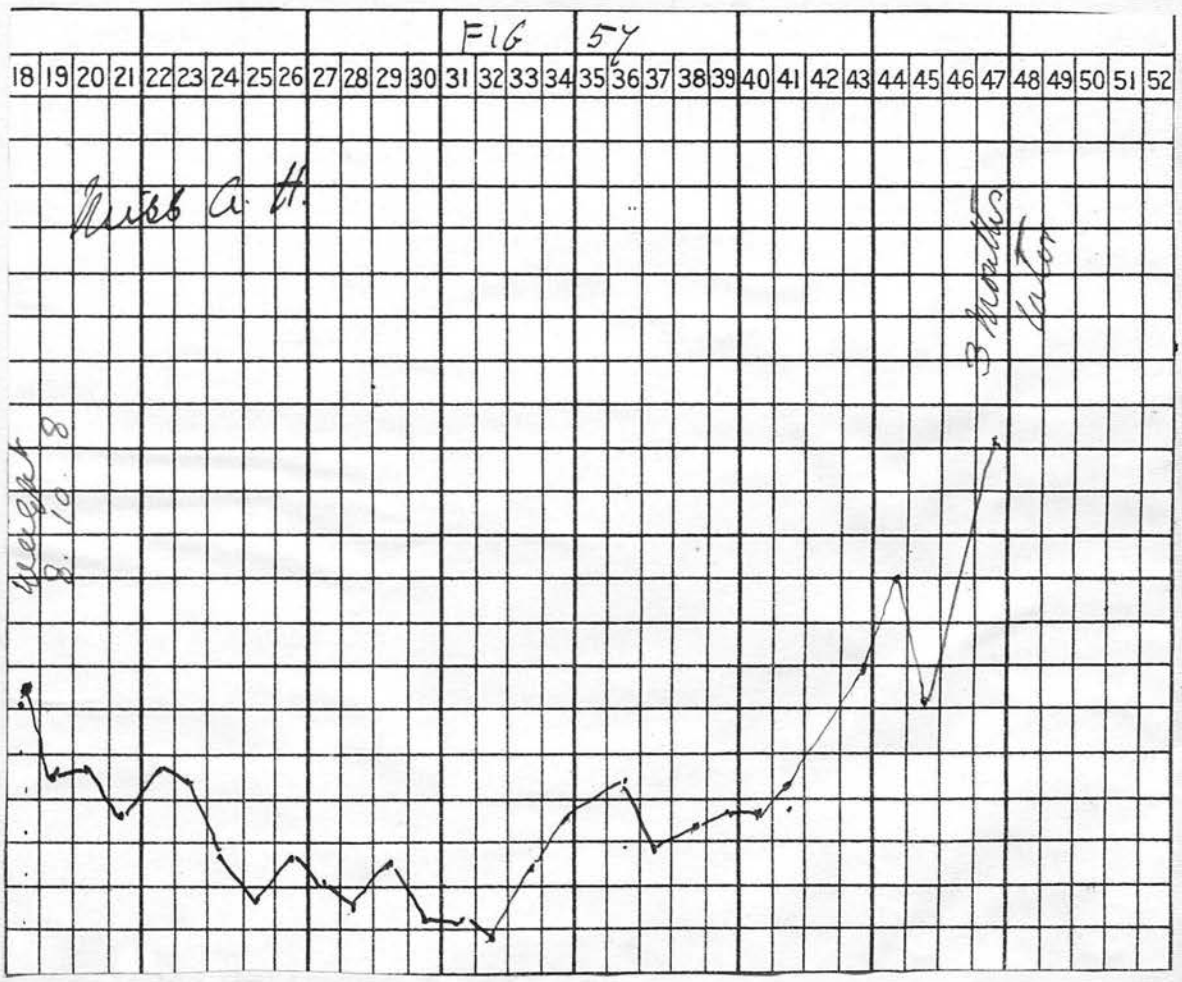
Physical examination: Crepitations right supra scapular region. Reacted to O.T. 001 to 100 Started with P.T.O. .003 to 101 Repeated dose; no reaction. Treated with P.T.O. P.T. O.T. up to 1. cc. She had reactions, but they did not appear to

affect her health, though for the time being she lost weight. Result: Discharged well. Saw 6 months later, had gained 6 lbs in weight since beginning treatment and appeared in absolute health.

The progressive loss of weight at the beginning was probably due to too rapid increase of the doses.

57

FIG. 51.



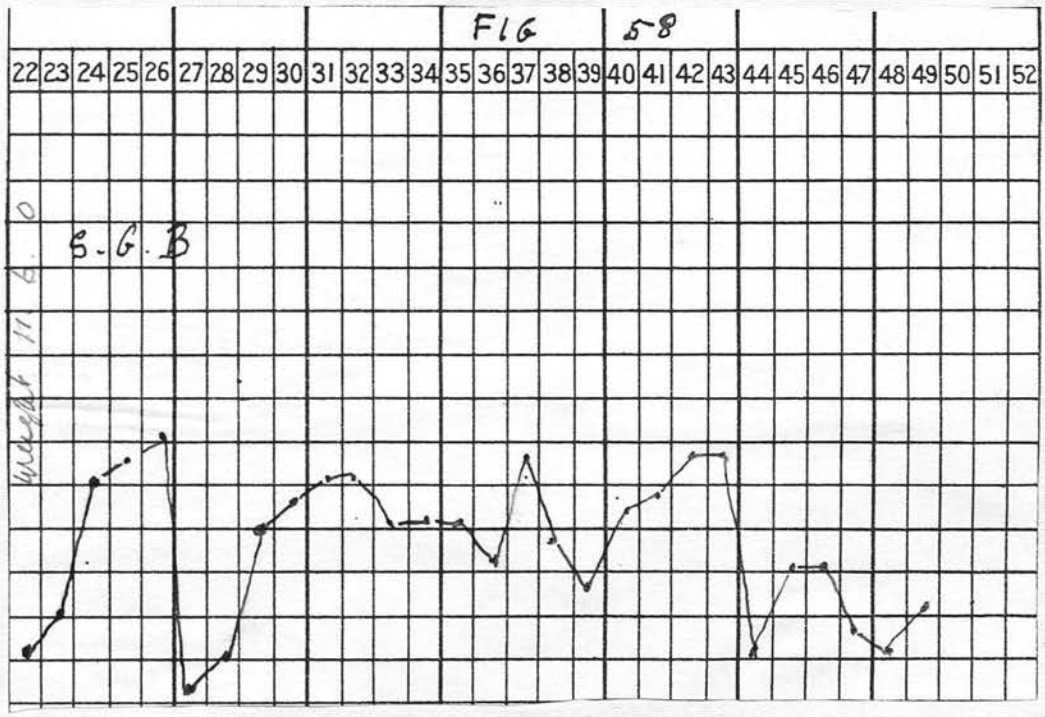
8. S.G.B. 30. 11. 10. '20.

History: Felt slack, especially in afternoon. Bad cough. Spits up "yellow". Red on handkerchief when blowing nose. Night sweats. Not lost weight. Neurasthenic.

Physical examination: Nothing in lungs. Liver enlarged. Reacted to 100 with O.T. 002. Treated with P.T.O. up to .7 then with P.T. up to .6 and then with T.A.F. up to 1. cc.

Result: Improved. Less neurotic. It will be noticed that he varied considerably in weight during treatment. 58

FIG. 52.



9. C.W.S. 20. 30. 8. '21.

History: Losing weight. Pain after food. Vomits after breakfast occasionally. Depressed. Sweats at night. Followed influenza a year ago.

Physical examination: Harsh breathing both bases of lungs. Stomach dilated. Tenderness on pressure left hypochondriac region. B.P. 130.

Reacted to T.A.F. .002 to 1c1. Pain in chest and stomach. Vomiting and headache. Waited a week. Began treatment with T.A.F. 0001 reacted to 101. Repeated dose twice, then became desensitized. Treated up to .75 T.A.F. FIG. 53. 59

Result: Very much better in every respect. Complete recovery of abdominal symptoms. Gained 7½ lbs in weight.

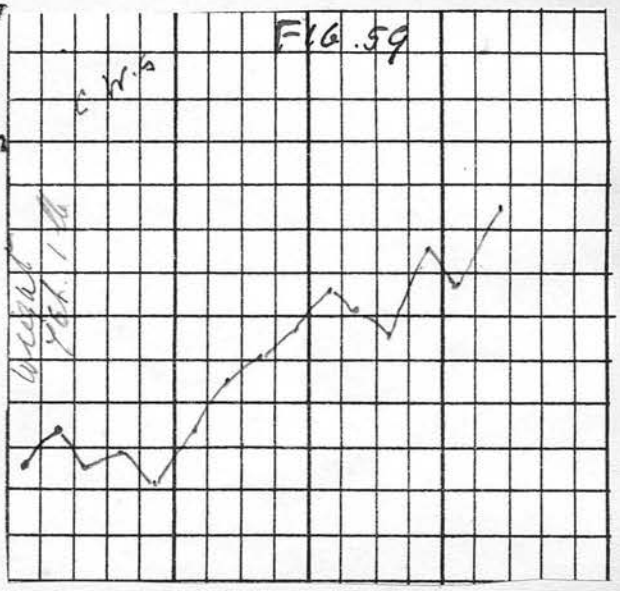


FIG. 59

10. Miss F.W. 26. 2. 12. '21.

History: Influenza three years ago. Lost weight since. Pain in lumbor region. Irregular menstruation. Easily tired.

Physical examination: Nothing to detect in heart, lungs, or abdomen. Hb 70. B.P. 120.

Reacted to T.A.F. 002 to 99 .8 Arm swollen; aching all over. Three days later gave T.A.F. 0001. No reaction, so doubled dose. Continued doubling up to .001 and then went more slowly up to T.A.F. 1. cc.

Result: Did extremely well. The treatment was entirely reactionless. Gained 3½ lbs and was much benefitted.

This was as nearly an ideal case as one could wish to undertake and is a fair model of the line of treatment at which we should aim.

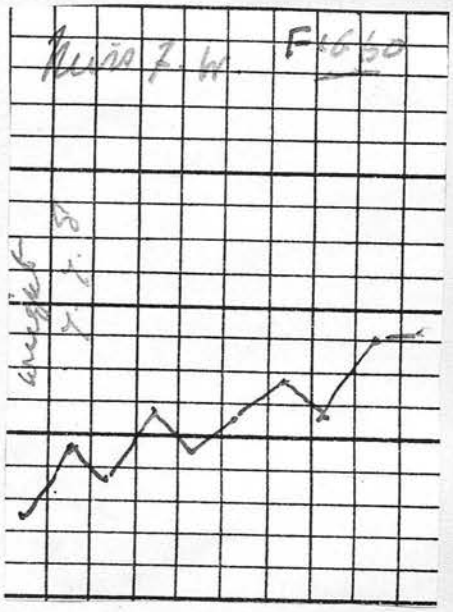


FIG. 54.

11. T.A. de H. 34. 5. 3. '21.

History: 12 years ago pleurisy. Went to Sanatorium, Midhurst, for 4 months. Since then colds in winter. Passed unfit for army in 1914. Haemoplysis energetic. No night sweats. No cough.

Physical examination: M.p. expectoration occasional crackle right base. Marked increased V.F. and Resonance.

Slight local reaction with T.A.F. 001. No rise of temperature with T.A. 002; rise to 99 ; repeated rise to 102.

Commenced treatment with T.A.F. 0001. No reaction. Doubled dose, no reaction. Gave .0004; slight reaction. Gave .0005; doubled, reacted, and then proceeded more cautiously up to T.A.F. 1. cc.

Result: Very much improved; able to play tennis and dance and

take long walks. Gained 2 lbs.

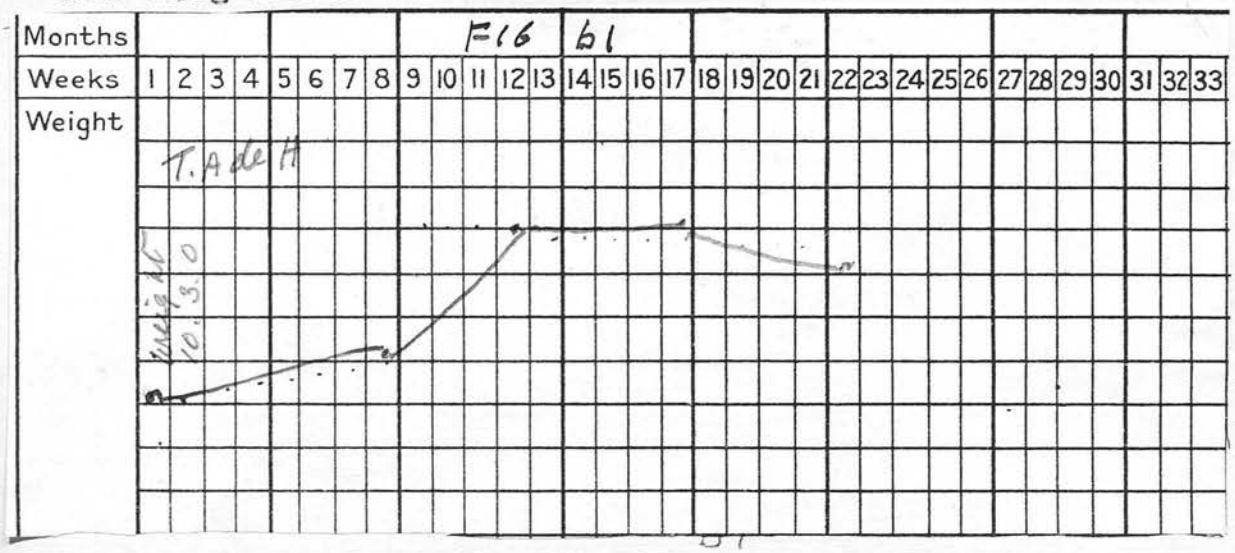
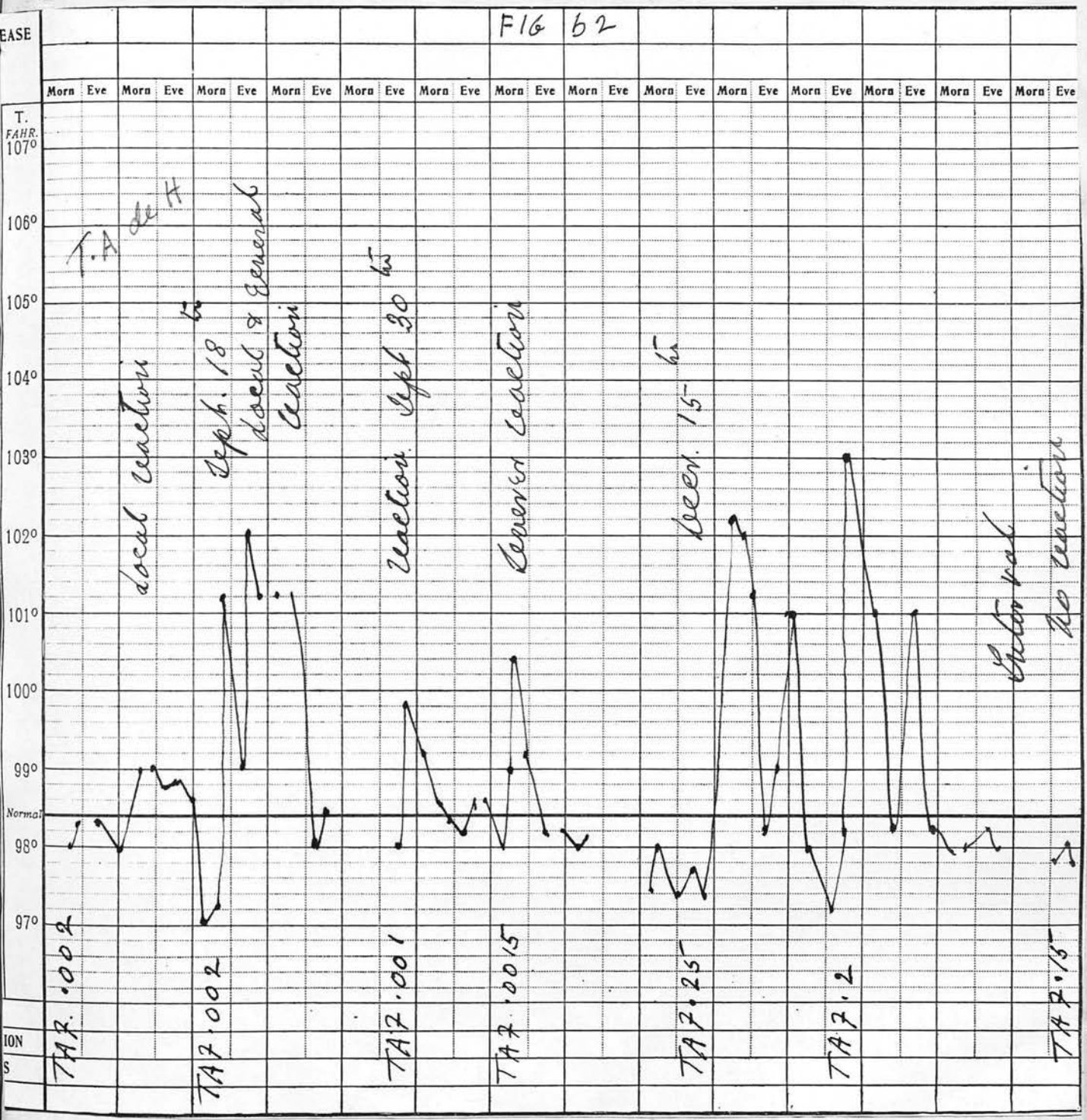


FIG. 55.

This case illustrates many mistakes.

1. He should not have been tested at all; his history was quite sufficient for diagnosis.
2. After a reaction with .001 the same dose should have been repeated, or slightly lessened.
3. When getting to so big a dose as .25 the reaction should have been respected and no dose given for a week or more.

The reactions did him no apparent harm, but I find that no good results, as a rule, and Inmow avoid them whenever I possibly can.



62

FIG. ~~56~~. T.H. de H.

12. Mrs R. 31. 19. 4. '22.

History: Pain in right side; worse at menstruation hemorrhage Indigestion. Flatulence. Nervy, inclined to cry. Slack pimples on face. Worse the last two years.

Physical examination: Artificial dentures. Tonsils enlarged. Enlarged glands neck. Harsh, rough breathing both apices. p 80. B.P. 120. Hb 70. clots badly. Liver a good deal enlarged. Weight 7. 4. 8.

Reacted to T.A.F. 002. Commenced treatment with .0001 and continued without reactions to T.A.F. 1. cc.

Result: Gained 2 lbs only, but all her symptoms gone and digestion practically all right.

This case illustrates what one so often sees, the clearing up of symptoms under this treatment.

13. F.W.G.M. 43. 5. 4. '22.

History: Vomited blood in army, invalided 1919. Operated on for appendicitis 20 years ago. Flatulence; pain over heart. Cough. White expectoration. "Blurring of eyes". "Throbbing after a meal" with pain. Gaining weight. Lost energy, especially in afternoon.

Physical examination: Rhonchi right side posteriorly. Dirty tongue. Stomach dilated. B.P. 145.

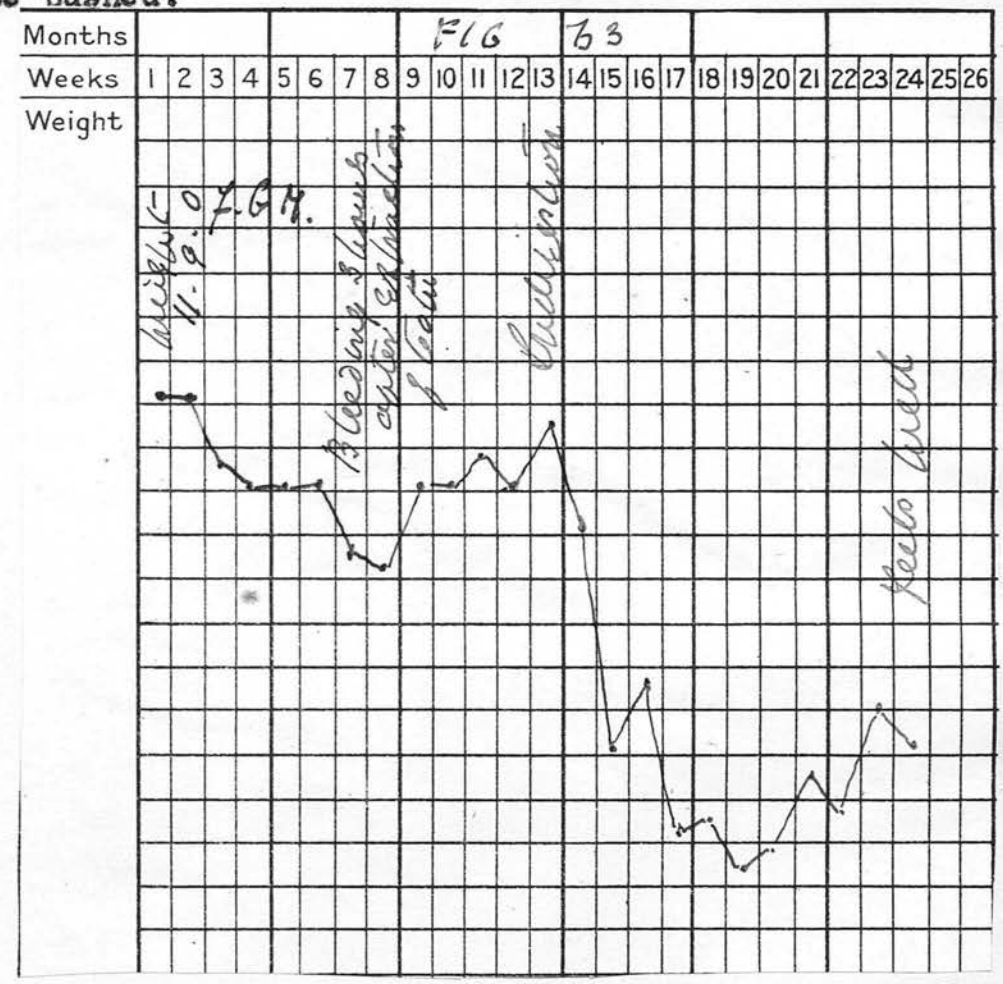
Reacted to T.A.F. 002. Started treatment with T.A.F. 0001. Treated up to 1. cc.

Result: Lost 9 lbs in weight, but this was to his advantage as he was too fat. Symptoms entirely disappeared and the result was most successful.

This is a good example of a "stable" case, in which Tuberculin can be pushed.

63

FIG. ~~57.~~



14. E.T. 37. 30. 3. '22.

History: Sister having Tuberculin haemorrhage 15 years ago. Certified as T.B. in 1914, in Sanatorium 3 months. Passed into army A.1. in '15. Served 2 years. Demobilized as A.1. Present condition: harsh breathing both bases. B.p.150. p 84.

Reacted to 103 with T.A.F · 002. Vomiting and naemoptysis. Treated with a detoxicated vaccine. Then commenced with T.AF. 0005 and rapidly increased without reactions up to T.A.F. 1. cc.

Result: This man has done very well. His chart is not recorded as it is misleading, as he was suffering at one time with abscesses which apparently affected his weight. He has now gained weight and is apparently a fit man. His case shews the pitfalls of testing in certain cases. The reaction was too severe to be justifiable.

Cases Reacting to 0003 and Over.

1. C.E. 36. 3. 10.'19.

History: Pain in back 3 days very anaemic. States attended Victoria Park 8 months on account of asthma.

Physical examination: Dental caries; stomach dilated. Nothing to detect in lungs.

Reacted to O.T. .004.

Treated with P.T.O. commencing with .001. Practically reactionless effects up to 1. cc.

Result: Gained 7 lbs. Very much improved.

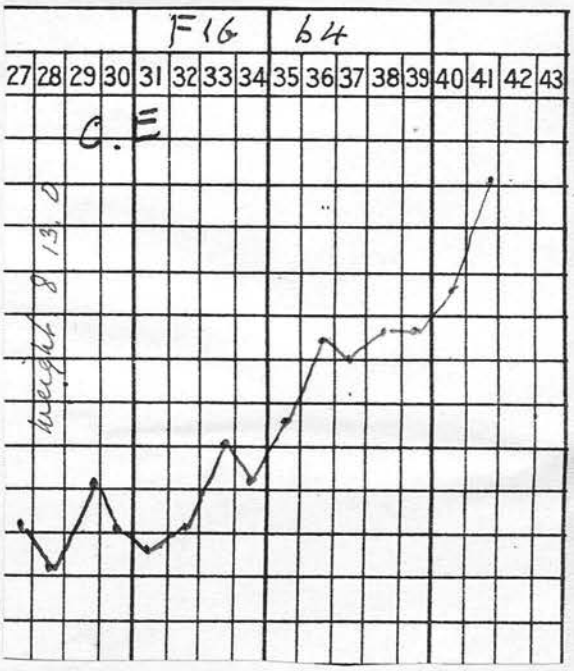


FIG. 58. 64

2. F.G.G. 41. 21. 1. '21.

History: For some weeks very slack; off food. Cough; trace of blood in sputum.

Physical examination: Deficient teeth. Glands in neck enlarged. Increased V.R. and V.F. both bases. B.P. 138. Weight 11. 10. 12. Reacted to O.T. 005 to 103 .4. Commenced treatment with P.T.O. 0005. Treated up to P.T.O. 1.cc.
Result: Did not go beyond this as felt perfectly well. Gained 2 lbs. No reaction.

3. Mrs K. 36. 17. 6. '20.
History: Influnaza 18 months ago. Since then run down. Sweats at night. Lost weight. Dysmenorrhoea.
Physical examination: Friction both apices.
Reacted to O.T. 004 to 101 .3. Commenced treatment with P.T.O. .001. Repeated 4 times as had reactions. Dropped to 0006; no reactions. Treated up to full dose of P.T.O. then O.T. and finished up with T.A.F. up to 1. cc.
Result: Feels very much better. Heard from her a year later to the effect that she feels in very good health indeed. There was practically no change in weight.

4. Mrs R. 38. 10. 5. '20.
History: Glands enlarged in neck for years. Old scars. Night sweats two months.
Physical examination: Friction right apex.
Reacted to O.T. 003; coughed, increase of night sweats.

Treated with P.T.O. commencing with .001 and O.T. up to .4.cc.

Result: General health improved; no change in weight. Would probably have done better, but owing to poverty did not get sufficient food. The treatment was reactionless and calls for no comment.

5. H.G.P. 22. 22. 4. '20.

History: Pains pit of stomach for some months. Worse after food. Tendency to "biliousness."

Physical examination: Nothing to detect in lungs. Liver enlarged. B.P. 110. Clots 6 to 8 minutes. Weight 11. 7. 12. Reacted to 100 with O.T. 003. Treated with P.T.O. commencing with .001, then with P.T. followed by O.T. up to 1. cc.

Result: Discharged well. Gained a pound in weight. Seen several times since, perfectly well.

This case gave no reaction and requires no comment.

6. T.C. 32. 20. 11. '20.

Pains in stomach for some time.

Physical examination: Harsh breathing both apices. Reacted to O.T. 003 to 103. Treated with P.T.O. commencing with .001, with P.T.C., T.A.F. up to 1. cc.

Result: All signs of dyspepsia gone; feels much better.

7. Rose S. Aged 14. 9. 11. '20.

"Always colds." Always eruption round mouth on and off since birth.

Physical examination: Apparently a healthy child.

Wassermann negative. Clots in 8 minutes. Reacted to O.T. 01 to 102. Headache; backache; eruption on face worse.

Treated with P.T.O. commencing with ;001 P.T. and T.A.F. up to 1. cc.

Result: Her colds were cured, but I cannot say there was any definite improvement in the eruption on the face.

8. Miss A.T. 26. 5. 1. '22.

History: Cough each winter. "Weak chest" Been in convalescent homes. Slack. tired.

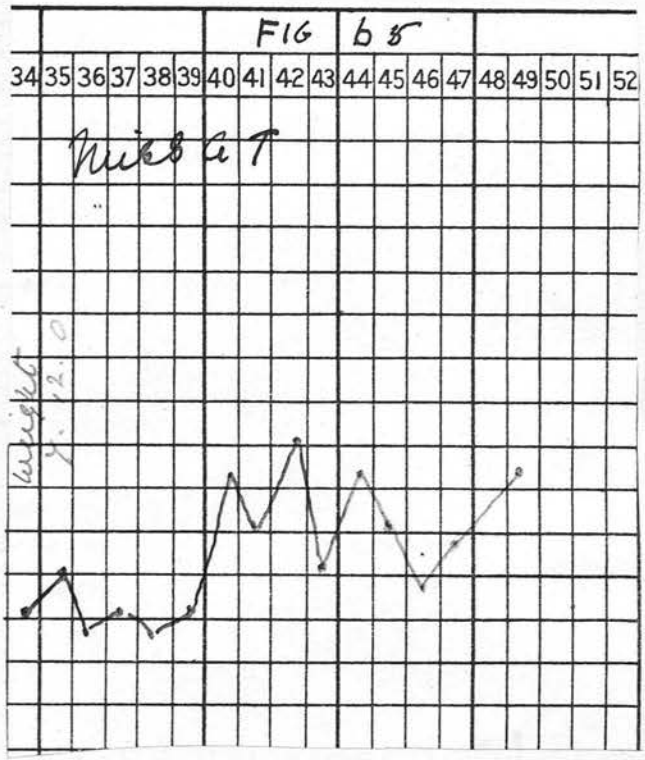
Physical examination: Harsh breathing both apices. Poor expansion. Liver enlarged. B.P. 120. Hb 70.

T.A.F. 0005 made her feel better; T.A.F. 001 no reaction. Gained 1 lb in weight. T.A.F. 005 arm was sore, cough increased, eating better. T.A.F. .007 reaction to 100 Arm sore, lost weight. Dropped to T.A.F. 0001; no further reactions and treated up to T.A.F. 1. cc.

Result: States used to have colds each fortnight; now none. Feels well in every way. Gained 3½ lbs. Saw 6 months after finished treatment, apparently well.

Treatment was reactionless.

FIG. 59.



The only adverse comment I can make on this case was that I pushed the test doses too far,

9. F.P.S. 28. 19. 7. '21.

History: Pain in stomach and right side 18 months. Vomits immediately after food (1 year). B. constipated. Night sweats. "Very run down."

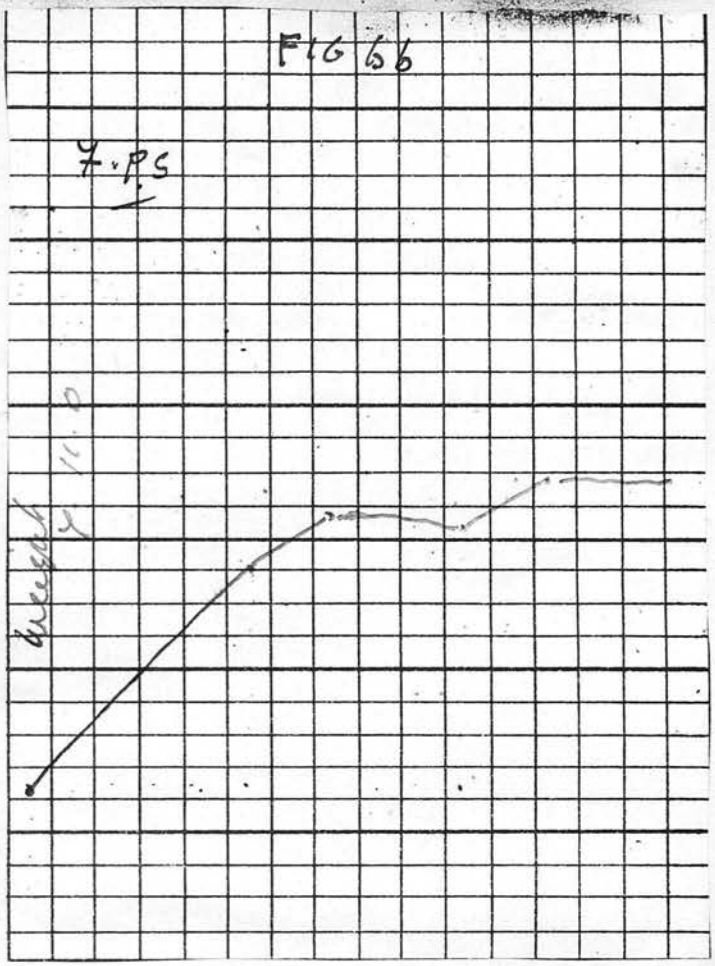
Physical examination: Paid on pressure over duodenum; otherwise nothing to detect. B.P. 120. p. 80. Very thin. During testing felt much better, but no reaction till T.A.F. 005 when reacted to 103. Waited a week, then gave him .0005 and rapidly increased to T.A.F. .1 cc.

Result: Feels absolutely well. Before treatment never 6 weeks on end without a week off. Saw 6 months later - not a day off work. Gained 9½ lbs

I pushed the doses very rapidly in this case. He was obviously subsensitive and he had no variations in morning and evening temperature.

66
FIG. ~~60~~.

F. P. S.

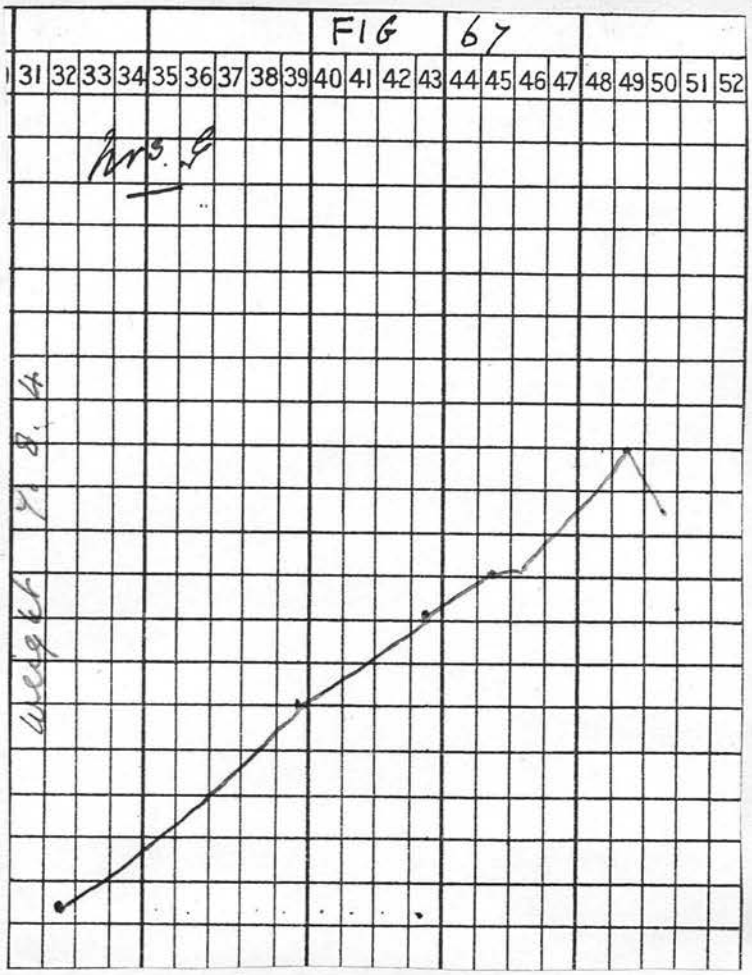


10. Mrs G. 48. 21. 10. '20.

Three months ago spat up blood. No cough. Pain middle back. Run down.

Physical examination: Glands in neck enlarged. Harsh breathing both apices with occasional crepitations. B.P. 140. Reacted to O.T. 006. Treated with P.T.O commencing with .001 up to P.T.O .02. Improved. Gained weight. Gave up. Recommenced treatment March '22., with T.A.F. .001 and continued up to T.A.F. 1. cc.

Result: Gained a lot of weight and was discharged feeling absolutely well.



~~67~~

FIG. 61.

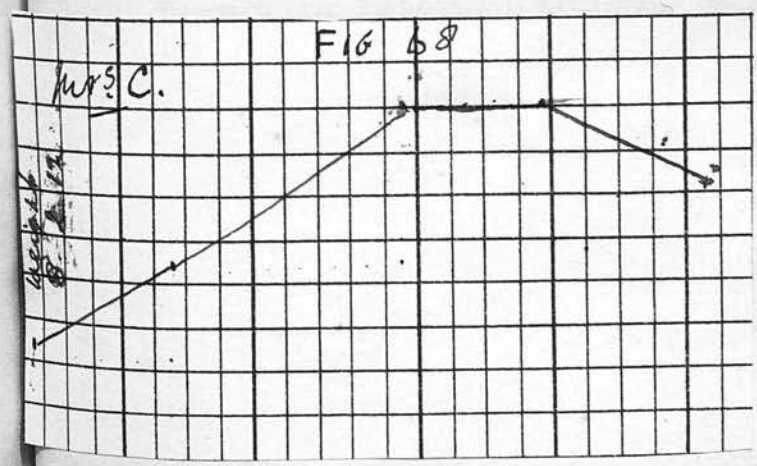
Mrs G.

11. Mrs G. 49. I. 1. '22.

History: Sleepy after work. Effort to get up. Rheumatism, sciatica; pain left side and in shoulder; very cold. Neurasthenic. Attended National Hospital for Epilepsy for nine years. Pneumonia and pleursy 3 years ago. Night sweats. Got thinner. Off food.

Physical examination: Nothing abnormal to detect. B.p. 120. Reacted to T.A.F. 01 to .101. Felt much better whilst being tested.

~~FIG. 62.~~ 68



Treated with T.A.F. commencing with 004 up to T.A.F. 1. cc.

Entirely reactionless.

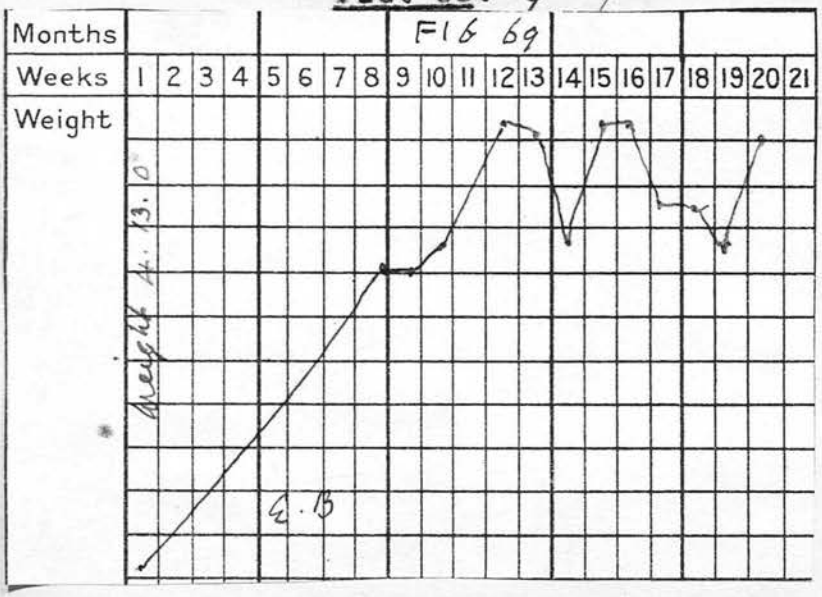
Result: Entirely lost neurasthenic symptoms. Felt quite well and gained weight.

12. E.B. 12. 32. 9. '21.

Never well. Bronchitis. Pain over heart. Night sweats.

Physical examination: Nothing to detect.

FIG. ~~65.~~ 69



Reacted to 100 with T.A.F. 01. Treated with T.A.F. beginning with 001. Rapidly increased in spite of reactions, as gained weight, up to 1.cc. Result: Absolutely well. Gained 10 lbs. 3 months later gained another 5 lbs

13. L. P. 43. 21. 3. '21.

Home with "stomach trouble" 3 weeks. Indigestion. "Black vomit." Told London Hospital Gastric ulcer; required operation.

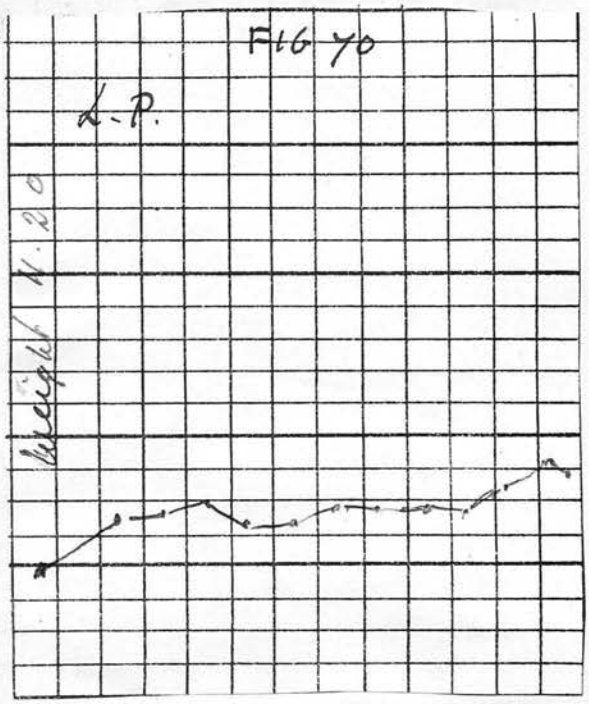
Physical examination: Stomach dilated. B.P. 120.

Reacted to T.A.F. 01 to 103, but felt better during test doses.

Treated with T.A.F. commencing with 0005, practically reactionless up to .25, then discontinued.

FIG. ~~64.~~ 70

Result: Symptoms gone; gained weight 2½ lbs. Saw 6 months later in good health.



14. Miss M. 18. 16. 12. '21.

History: Headaches. "Anaemia" a year ago. General health fair. "Lazy."

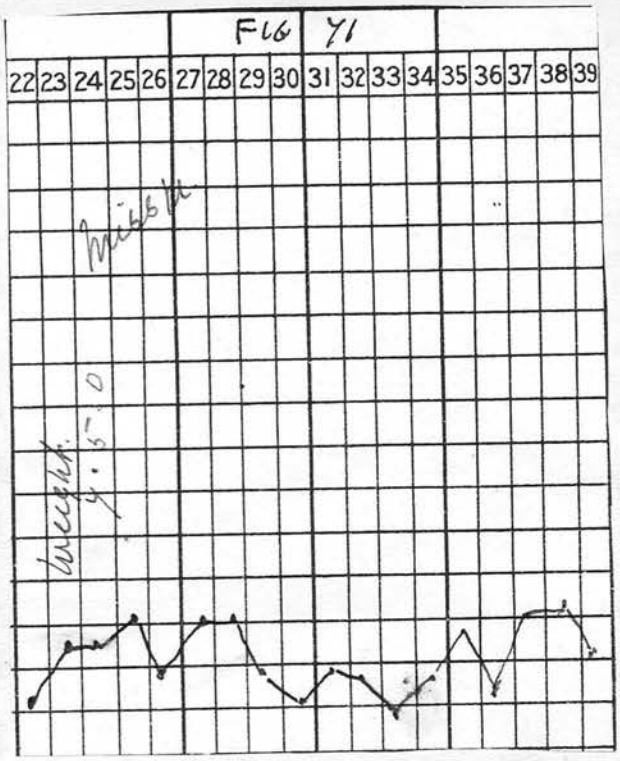
Physical examination: Expiration prolonged both apices. Stomach dilated. B.P. 130.

Reacted to 100 with T.A.F. 004. Treated with a detoxicated vaccine up to .1 Then commenced with T.A.F. 001 and rapidly increased without reactions up to .2 when she went on a holiday.

Result: Her mother wrote to say that "she wished her to continue the treatment which had done her so much good in every way, but she refused as she is feeling perfectly well." Weight remained stationary.

FIG. 65. 71

Miss M.



15. Mrs P. 31. 21. 1. '22.

History: Tired; slack; off food; nervous.

Physical examination: Glands neck enlarged. Expiration prolonged both apices. Liver enlarged. Blood pressure 120. Hb 80. Reacted to 100 withT.A.F. 003. Commenced treatment with .0005 and rapidly increased up to T.A.F. 1. cc.

Result: Felt very much better. Did not gain weight at time, but 4 months later had gained 4 lbs.

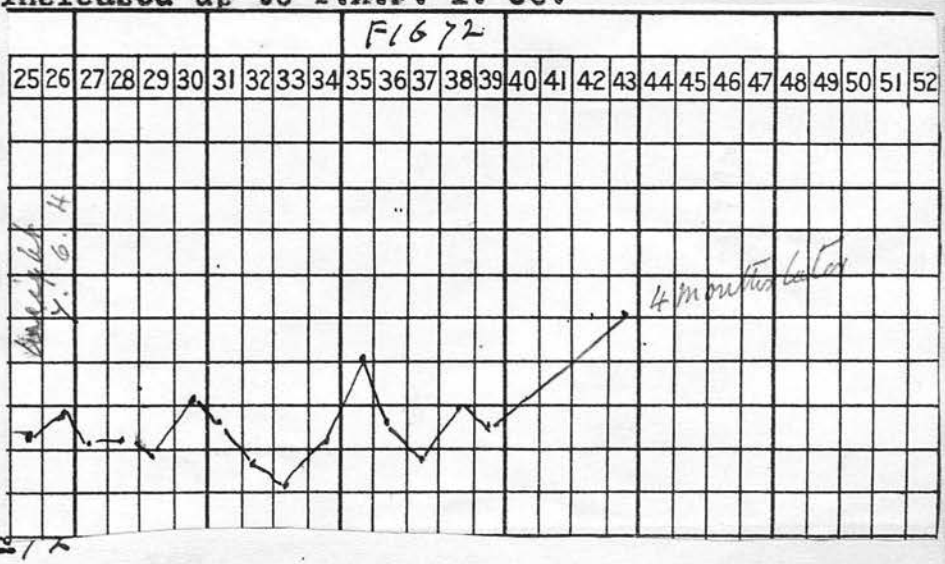


FIG. 66. 72

16. Miss M.P. 33. 2. 1. '22.

History: Influenza three years ago. Since then catarrh. This year colds on chest. "Choking," in morning. Tired; weak.

Physical examination: Harsh breathing right apex. Stomach very dilated. B.P. 130. Hb 80. Very neurasthenic.

Reacted to T.A.F. 003 to 100. Treated with T.A.F. commencing with 0001; practically reactionless throughout. Treated up to 1. cc T.A.F.

At times, when the catarrh was bad, I gave her small doses of detoxicated coryza vaccine combined with T.A.F. with great benefit.

Result: Her weight remained fairly stationary 7. 4. - 7. 6. throughout, but she stated that she felt very much better, far less nervous and not suffering from catarrh.

16. T.H.R. 33. 26. 6. '20.

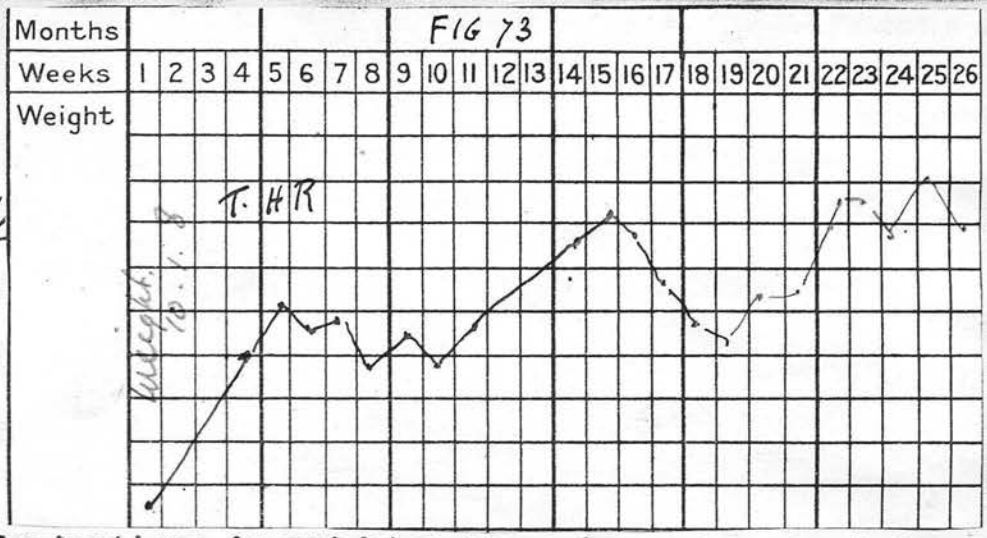
History: "Tired." Nervous. Bad family history.

Physical examination: Harsh breathing both apices. Increased vocal resonance right base. p 90. B.P. 138.

Reacted to 100 to O.T. 003; gained 4½ lbs during testing.

Treated with P.T.O. commencing with .001 up to .7; then with P.T. which suited him well, and then with O.T. up to 1. cc.

Result: Feels very well indeed; gained over 6 lbs in weight.



73

FIG. ~~67~~.

T. H. R.

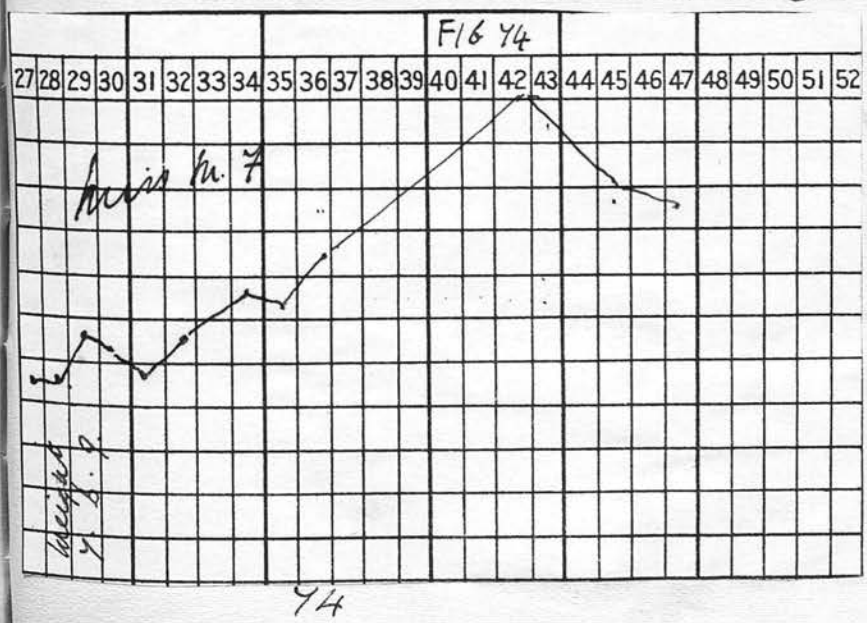
The fluctuations in weight more or less corresponded to reactions. This was one of my early cases. I now avoid reactions as much as possible.

17. Miss M. F. 29. 31. 8. '21.

Tired on exertion. "Yawns"; depressed; headaches; pains back neck; cough. Lost weight for two years.

Physical examination: Crepitations friction apices back and front. Stomach dilated. B.P. 130. Hb 70%.

Reacted to T.A.F. 005 to 100. As gained weight, started treatment with T.A.F. 001. Slight reactions, but improved steadily. Gave up to 1. cc



74

FIG. ~~68~~.

Result: Felt very well. gained 5 lbs.

I think in this case I pushed the treatment rather far, as she began to lose weight with the bigger doses. I saw her, however, 6 months later and she appeared in excellent health.

18. Miss M.S.T. 53.

History: Rheumatism when a child. Nervous, run down; result of septic poisoning. Headaches, feels sick. Rheumatic pains; Slack, lazy, asthma.

Physical examination: Friction right apex posteriorly. B.P.120. Reacted to potatoes and feathers, so cut her off these. Reacted to T.A.F. 003 to 100, She was obviously non-sensitive so I continued treatment from that dose up to 1. cc.

Result: Stated it was the first year she hadn't had asthma for 4 years. Her general health was greatly improved and the rheumatism very much less.

19. C.T. 33. 8. 1. '22.

History: 5 years ago fell off bicycle, displaced cartilage. Cartilage removed from right knee in 1918; all right till last August, then sinorites. Knee tapped twice a year. Fluid examined for T.B; result negative. Constantly laid up on account of knee. General health poor. Depressed.

Physical examination: Considerable lateral movement in right knee, but no effusion. B.P. 130. Ordered a "Hawksleys Splint" for knee.

Reacted to 104 with T.A.B. 003. Started treatment with T.A.F, 0001 and pushed doses in spite of reactions as he was improving so much, up to 1. cc.

Result: Felt absolutely well at the end. Not had knee cap on for the last 6 weeks and is able to walk for miles.

20. E.C.G. 35. 12. 8. '22.

History: Influenza. General break down. Swelling both feet, hands and wrists.

Physical examination: Marked rheumatoid arthritis and fibrositis finger joints. Bad psoriasis of forearms and a nervous wreck. Stomach dilated. Blood pressure 110.

Reacted to T.A.F. 006 to 100. Commenced treatment with 000 T.A.F .000001 and rapidly increased up to 1. cc. Entirely without reactions.

Result: In his case Tuberculin seemed to act like a charm. The pain, swelling, and stiffness has entirely left him. He eats well and the psoriasis which was very chronic, has nearly disappeared.

Miscellaneous Cases.

Under this heading I shall describe cases which it was considered unnecessary, or undesirable, to produce a classical reaction.

1. Edith J. 14. 25. 6. '22.

History: Lost weight; off food; restless; feels the cold; Slack.

Physical examination: Dental caries. Harsh breathing both apices. L.V.R. right base. Liver enlarged. B.P. 110. p. 90. Hb 80%. Clots badly.

Arm slight red at T.A.F. 004., eating better, gained weight, increased to 005., 006., and so on up to 1. cc. No reactions throughout.

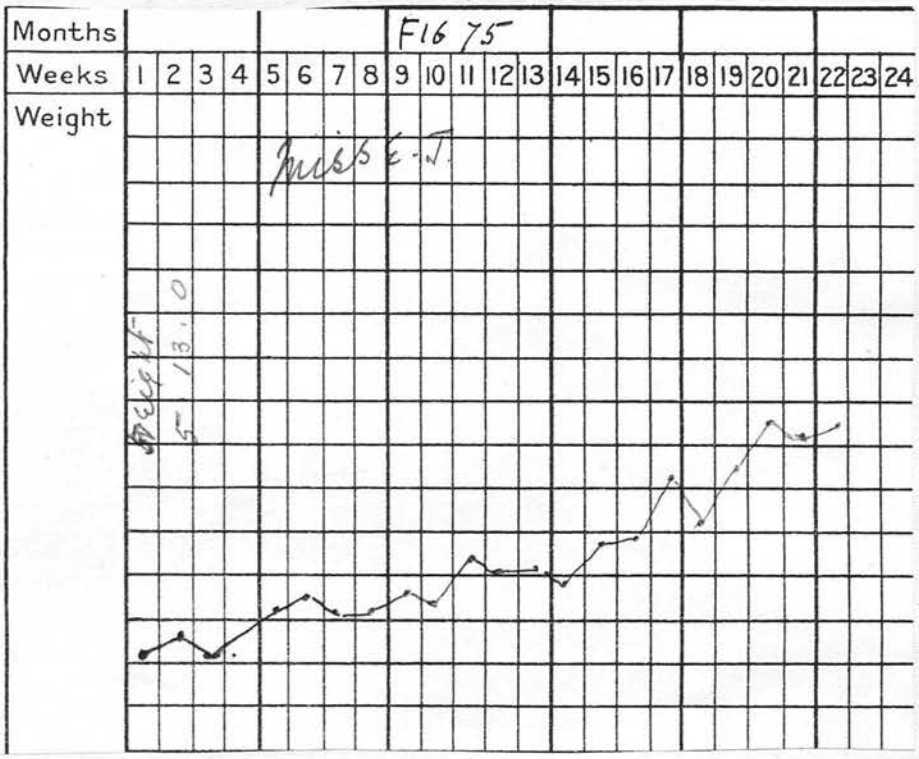
Result: Very much better, gained 5½ lbs.

I here made my diagnosis on the improvement occurring during testing.

75

FIG. ~~69~~.

Edith J.



Mrs M. 40. 29. 1. '20.

History: Influenza. Night sweats. Cough.

Physical examination: Loud systolic at apex, crepitations both bases.

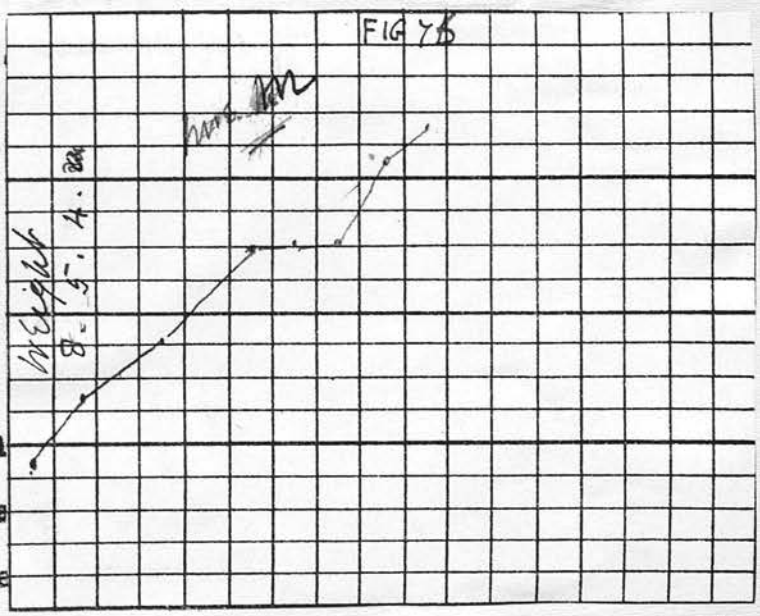
Commenced with P.T.O. 0002

Repeated dose in a week and gradually increased.

No further reactions.

Treated up to P.T.O. .035 when discontinued as she stated she felt quite well

Gained 7½ lbs. This case illustrates the great bene fit that is sometimes derived by small doses carried on for a limited time.



76

FIG. ~~70~~.

Unfortunately one doesn't often come across them.

3. Gracie C. aged 6. 21. 1. '21.

History: Constant colds, never well. Appendix removed London Hospital. No appetite. Cough. Dirty tongue.

Physical examination: Friction left flank; vales all over left lung. Hb. 70% Coagulated in 8 minutes. Tested with P.T.O. commencing with 0001 P.T. and T.A.F. Treat up to 1. cc Practically reactionless; treatment interrupted by colds.

Result: Gained 4¼ lbs. Quite well and free from cold.

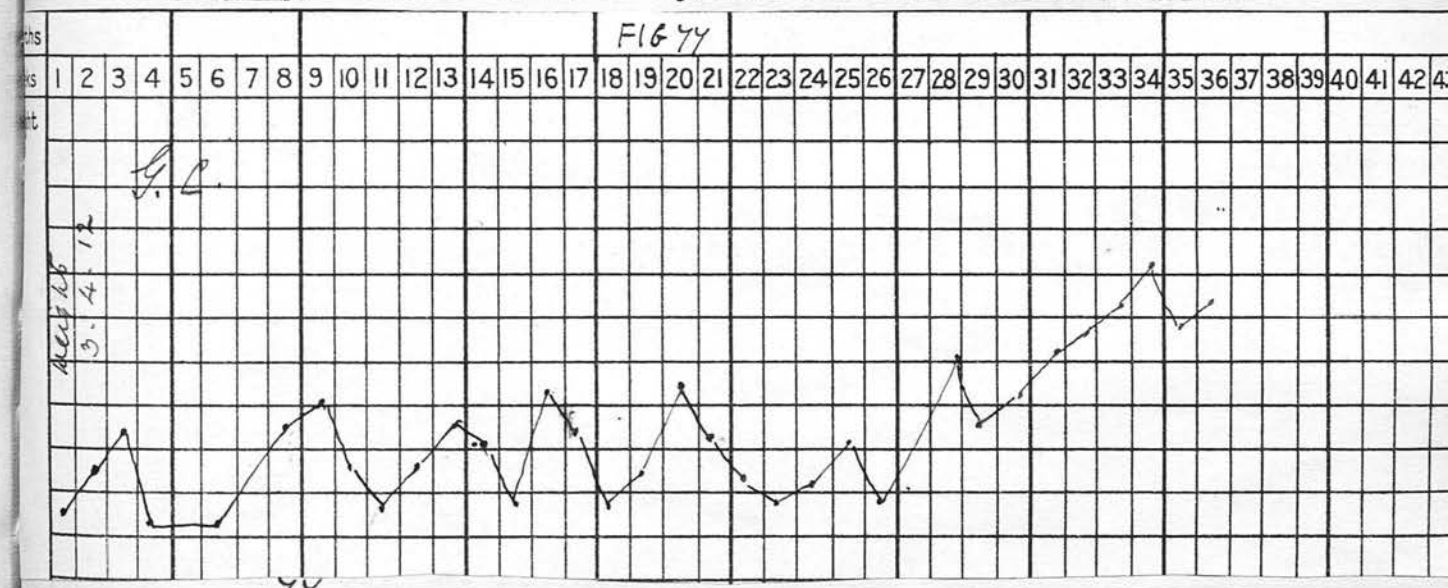


FIG. ~~71~~.

Note gain in weight with higher doses.

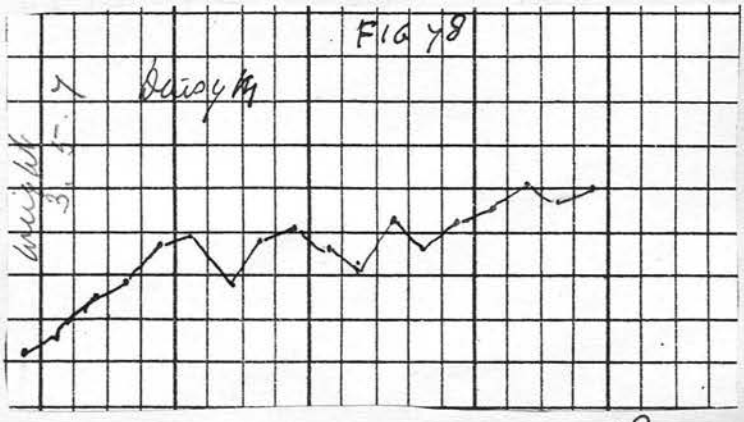
4. Daisy M. 7. 20. 1. '22.

History: Colds since a baby every three weeks. Night sweats; breathless. Can't run. Excitable. Sleepless. Got thinner.

Physical examination: Nothing definite in lungs. Stomach dilated. B.P. 90.

No reaction up to .01 T.A.F., but gained weight. Doubled doses up to ½. Then had slight rises of temperature, so went more cautiously. Had occasional colds so gave catarrhal vaccine along with T.A.F. with apparent benefit. Treated up to 1. cc. T,A.F.

Result: Did extremely well, gained 4½ lbs. Saw 6 months later, health maintained.



This is a type of case you sometimes meet in which a patient seems to respond at once to Tuberculin without giving any reaction. FIG: 78.

5. A.P. 37. 3. 1. '20.

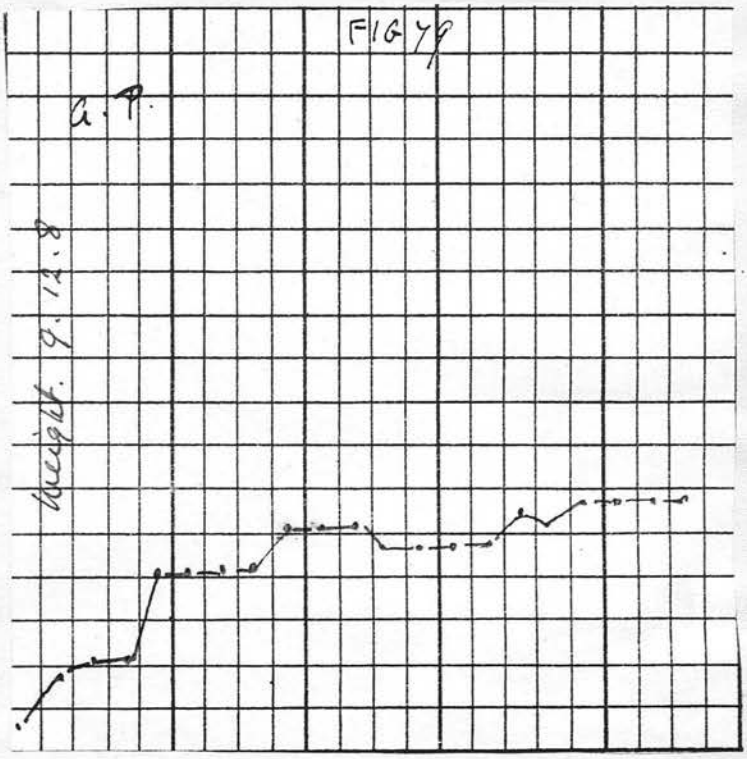
History: Rheumatic fever twice. Pains across back; night sweats.

Physical examination: Signs of consolidation both bases. Commenced with P.T.O. 0005, gave sewere reaction, but felt well. Very shortly was desensitized. Gained weight all the time. Treated with P.T.O. P.T. and O.T. up to 1. cc.

Result: Gained 5 lbs and felt very well. A year later given a short course of T.A.F. Stated better after 2nd course than after 1st.

FIG. 75. 79

This was one of my earliest cases when I did not pay so much regard to reactions as I do now.



6. Mrs. H. 42. 6. 12. '19.

This case is one of particular interest to me. It is the first case I dealt with and I was kindly "spoon fed" throughout by Dr Camac Wilkinson. i.e. - He measured out the doses for me and let me administer them myself.

Examination by Dr. Wilkinson.

Right lung stage II Left stage II. III.

Commenced treatment with P.T.O. 001; no reaction. Then P.T.O. .0013, reaction to 100 Dose repeated, no reaction; gained weight. Then 0017; rise of temperature. Dose repeated and so on up to O.T. 1. cc.

Result: Very well; able to resume work in open air school as a teacher. Physical signs appeared to be those of a healed lesion. Saw 6 months later; gained 5 lbs. Very well, not a day off work.

If a grateful pupil may presume to criticise his teacher, I would venture to suggest that the doses were pushed too rapidly. Whatever one's theory is as to the action of Tuberculin, I cannot believe that progressive loss of weight, even with no reactions, is a favourable sign. It does not appear to me to justify increase of dosage. The result, of course, justifies the means, but now I should go much more slowly. I don't look upon weight as everything, but in a woman with an initial weight of 6. 8½ it is a serious consideration.

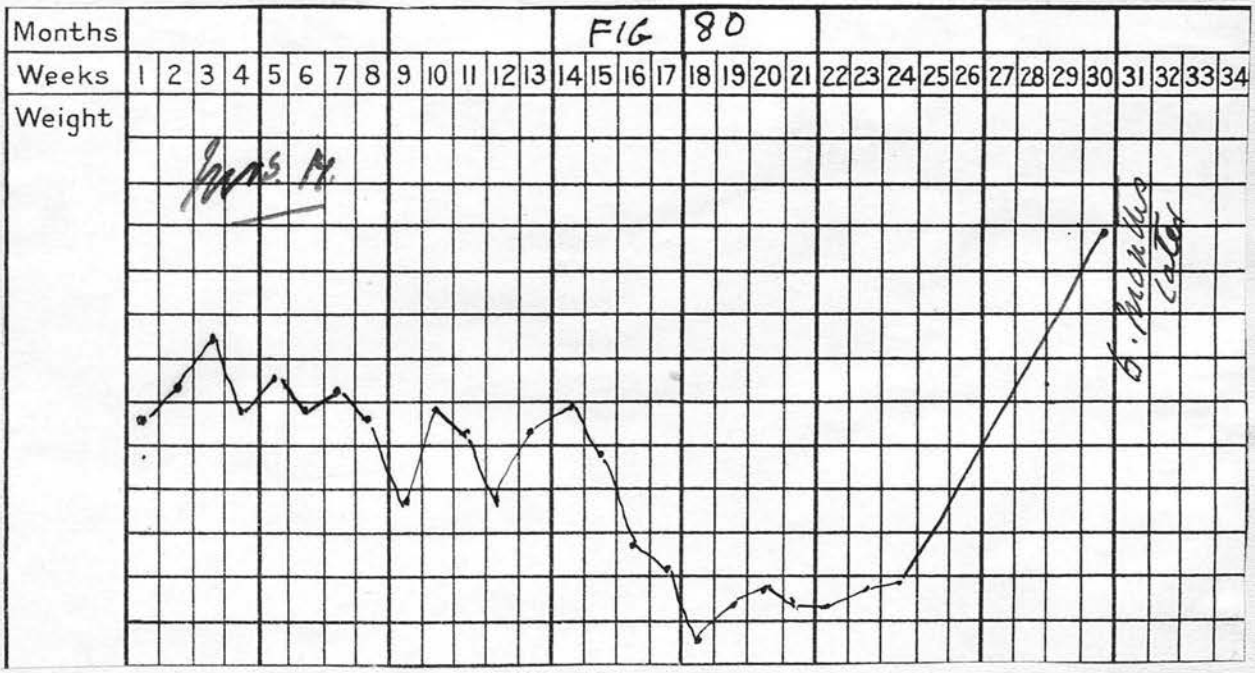


FIG. ~~74~~.

7. E.G. 30. 10. 2. 20.

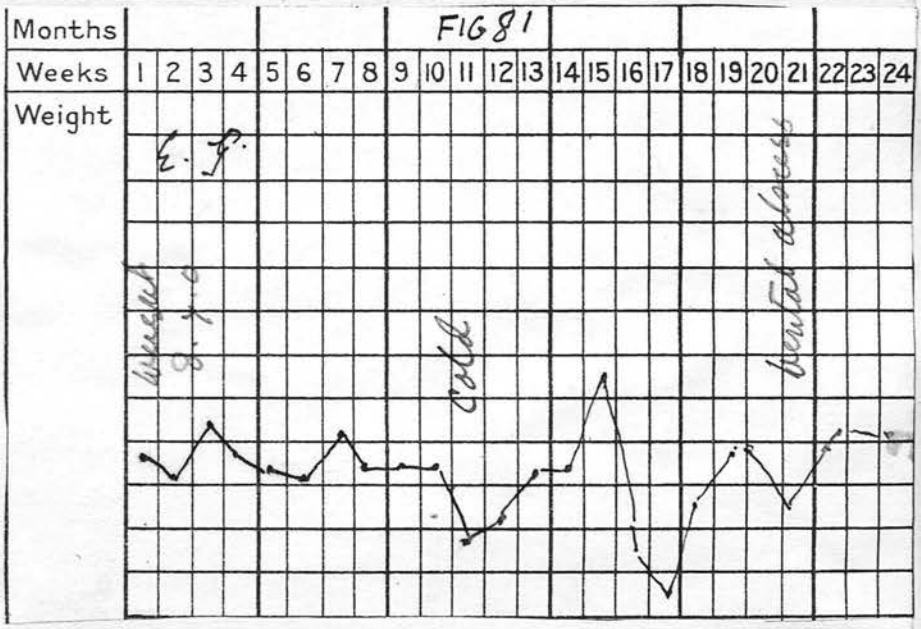
History: P. of war in Germany;, contracted dysentry. Since then pains in arms and legs, and looseness of bowels. Depressed. Cough. Indigestion.

Physical examination: Poor expansion of chest. Harsh breathing both apices.

Treated with P.T.O. commencing with ;0004, P.T. and O.T. up to 1. cc. No reactions.

Result: Felt very much better. No gain in weight. Saw a year later; Never sick since treatment. This case is not a conclusive one.

81
FIG. ~~75~~.



8. J.A. 45. 25. 9. '20.

History: Cough for 20 years, yellow expectoration. Spits blood. Good appetite; depressed; worries. At a Sanatorium 10 years ago.

Physical examination: "Crackles" left apex. p 72. Liver enlarged. B.P. 110.

Commenced treatment with P.T.O.0002 Treated without reactions with P.T.O. P.T. and O.T. up to 1. cc.

Result: Felt very well. Could detect no abnormal signs in lungs at end of treatment.

2 years later cough returned, but cleared up entirely under a short course of T.A.F.

N.B. This man persistently refused to be weighed throughout the course.

9. J.C. 28. 10. 11. '20.

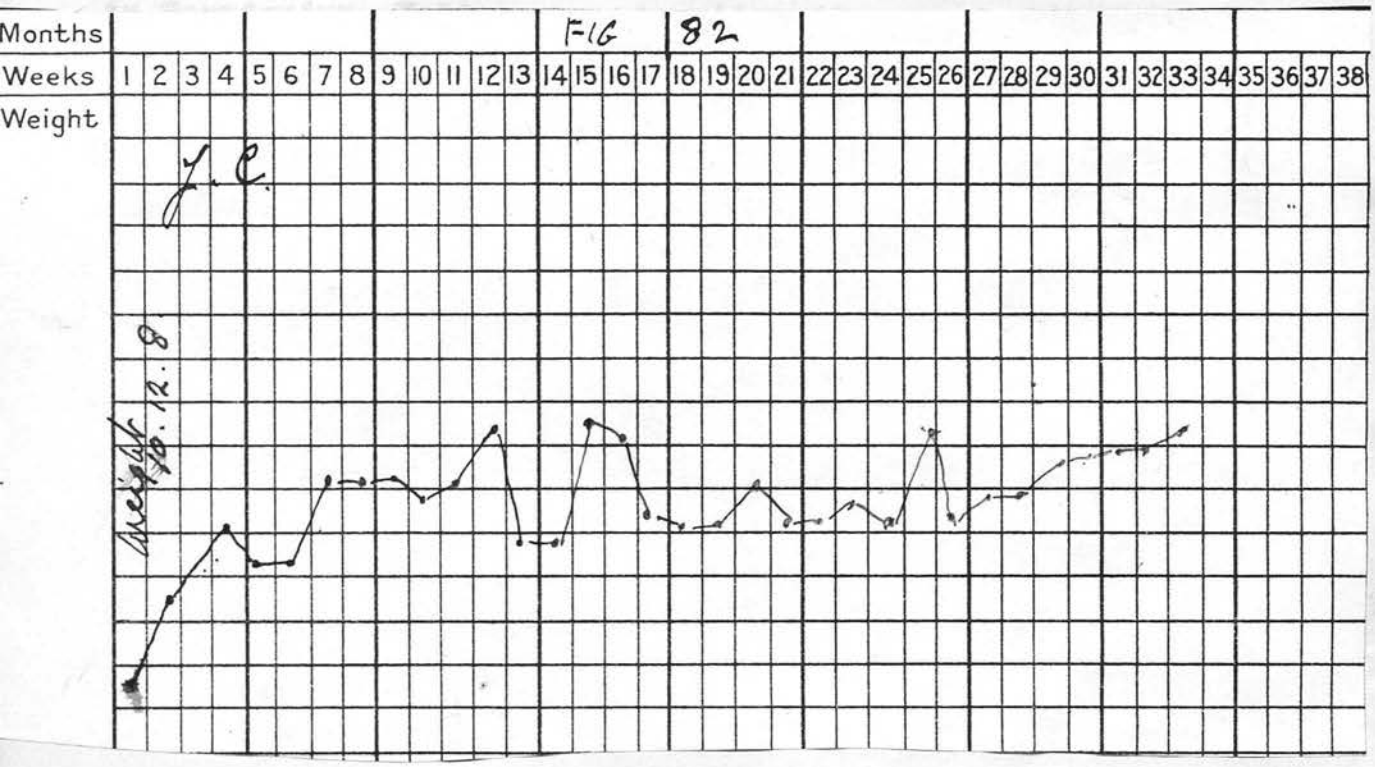
History: Bruised left testicle in France. Later removed on account of T.B. Peroneal abscess followed; now right testicle affected. Pain passing water.

On Examination: Right testicle obviously affected. There is a sinus in perineum connected with urethra. Friction right apex of lung.

Treated with P.T.O commencing with .0004, then P.T. and then O.T. up to 1. cc.

Result: Gained 5 lbs in weight and was able to return to his work on the railway and appeared in splendid health.

A year later he came to me in a very bad condition. The sinus which had healed broke down again. He had bad kidney trouble and he shortly afterwards died of nephrites.


Months
Weeks
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38
Weight
FIG 82
J.C.
Weight 10. 12. 8.

82

FIG. ~~76~~.

J.C.

10.E.P.N. 37. 1. 6. '21.

History: Double pneumonia and pleurisy last November. 3 months in Sanatorium. Yellow expectoration 40 ozs per diem. Slack. Bronchitis each winter.

Physical examination: Rhonchi back and front both sides. B.P.130. Commenced treatment with P.T.O. 00004. This gave reactions, so treated with a detoxicated vaccine up to .4 cc. Lost weight, but temperature was steady. Able to start work. Later gave T.A.F. beginning with .001 up to 1. cc.

At end of treatment no signs at apices, harsh breathing bases and occasional crackles.

Three months later came back again, stating he missed the treatment. I again put him on large doses of T.A.F. which stimulated him up for the time.

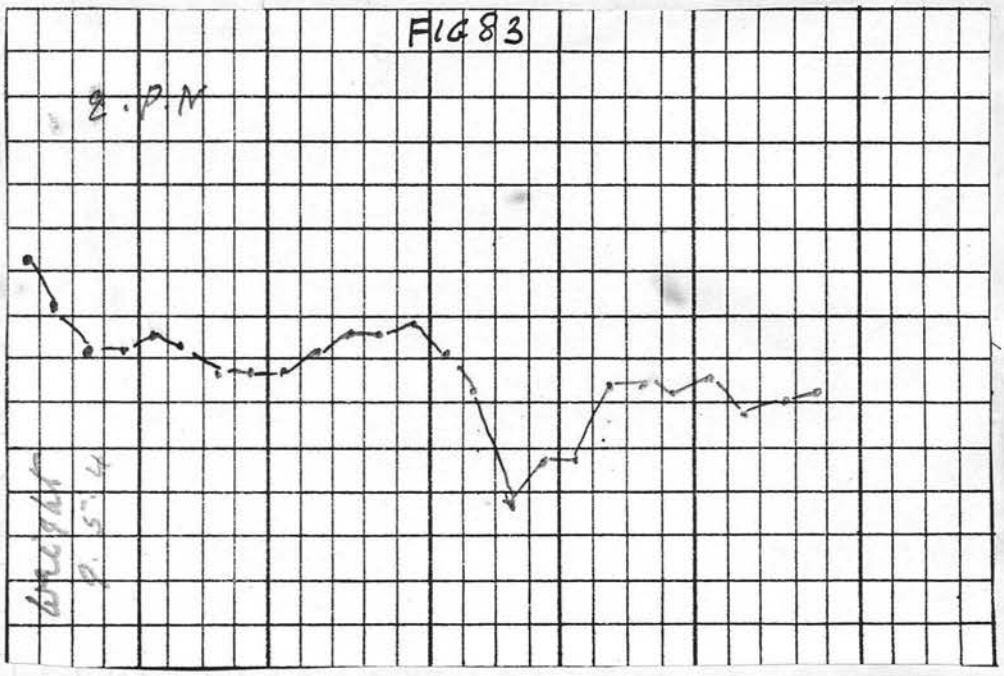
In January '23. I saw him in bed with vales all over his chest.

Result: Tuberculin seemed to do this man temporary good, but there is no evidence of permanent benefit.

83

FIG. ~~77~~.

E.P.N.



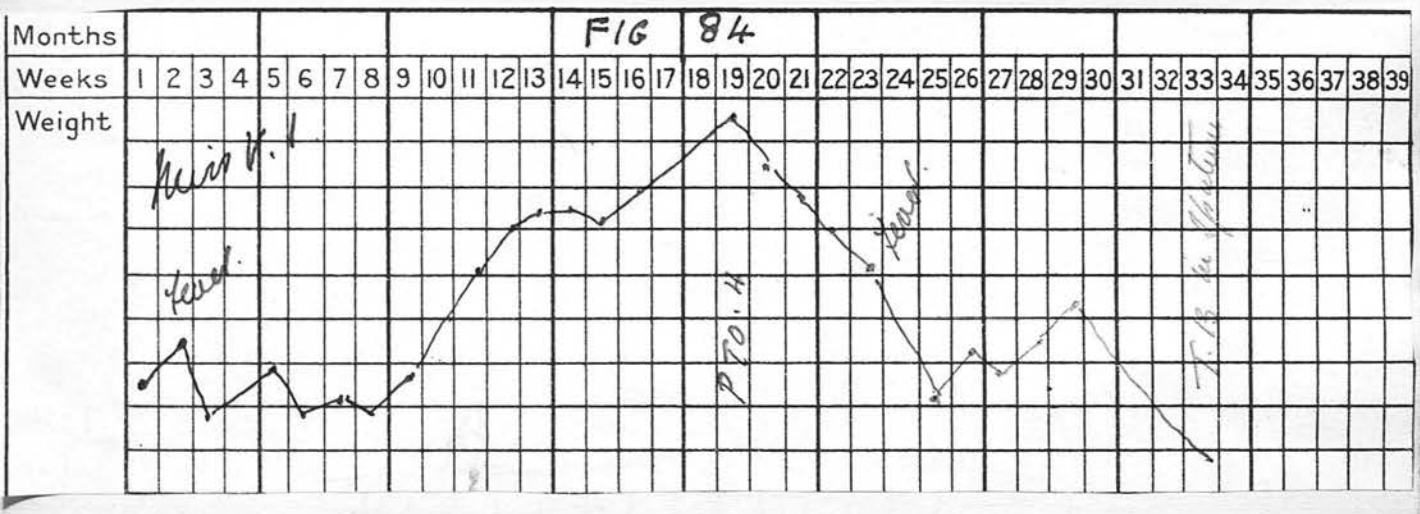
Cases With T.B. in Sputum.

1. Violet I. 20. 1. 5.'20.

Cough; very weak; night sweats. Bronchi both apices crepitations base. T.B. in sputum. Sanatorium.

Treated with P.T.O. commencing with 0002, P.T. and T.A.F.

Result: She very much improved in general health, but lost a lot of weight. At end T.B. in sputum.



84

FIG. ~~78.~~

I cannot call this a favourable case; as will be seen she gained a lot of weight for a time. I do not consider the treatment did her harm, but it did not do her much good. The whole of her family died of tuberculosis.

T.H. 28. 31. 3. '21.

History: All family except himself died of T.B. in 6 weeks night sweats.

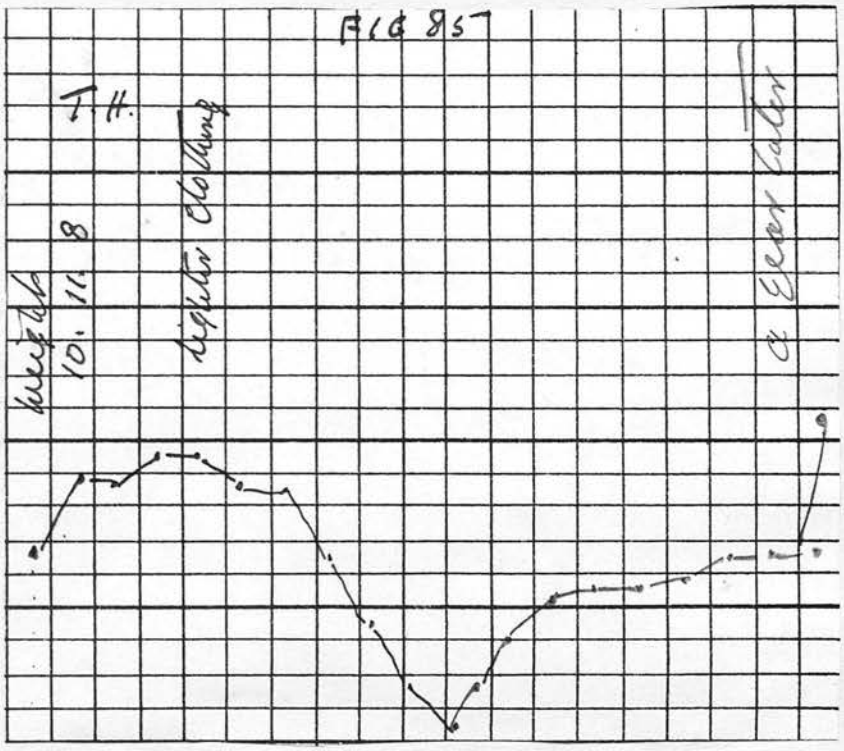
Physical examination: Harsh breathing both lungs posteriorly, especially at base. T.B. sputum.

Treated with P.T.O., commencing with 0005 P.T. and T.A.F. up to 1. cc.

Result: T.B. negative. Works up till 12 midnight and feels quite well. Gave a second course a year later.

85

FIG. ~~79~~.



There was a steady fall in weight during early part of treatment, but he looked and felt well, but, as is seen, he regained weight later on.

3. A.M. 48. 13. 7. '21.

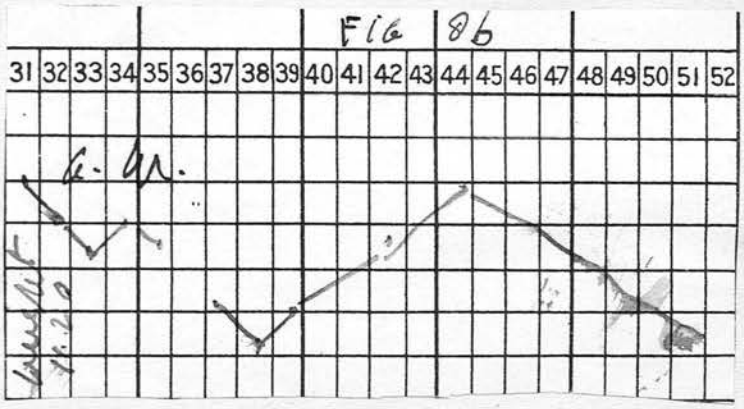
History: 18 months in Sanatorium. T.B. and Heart trouble, pleurisy twelve months ago, and again in Sanatorium. Loss of appetite; cough; night sweats; weak.

Physical examination: Deficient expansion and bronchi both bases. B.P. 130. p. 72.

Commenced treatment with P.T.O. 0002; rather severe reaction. Then treated with a detoxicated vaccine, which gave slight reactions up to .2. cc. Then gave T.A. 001, which was pushed up to .5 cc.

Result: He had general slight hemorrhages, lost some weight and did not appear to benefit much by the treatment. I don't think the fault lay with the dosing, but he was a traveller and took too much exercise in bad weather.

FIG. 86.



4. Mrs I. Mother of Violet I. 56. 10. 10. '19.

History: 7 children alive, 7 dead. 2 miscarriages. Uterus removed two years ago. Never right since then. Pain left side; cough; losing weight; night sweats.

Present condition: Crepitations both apices. T.B. in sputum. Treated with P.T.O., commencing with 0002; then P.T. and then O.T. up to 1. cc. No reactions.

Result: Much improved for the time, but at the end T.B. was still in the sputum. A year afterwards died of nephritis, probably the result of a tubercular kidney.

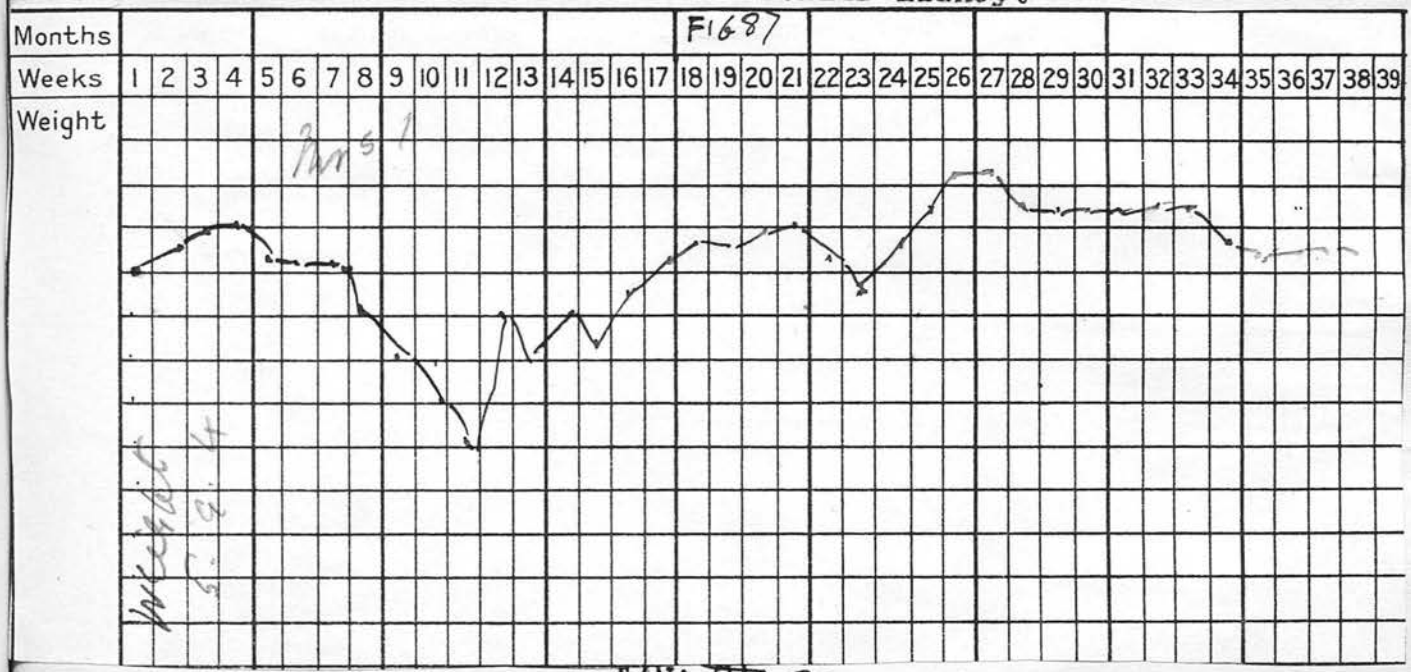


FIG. 82. 87

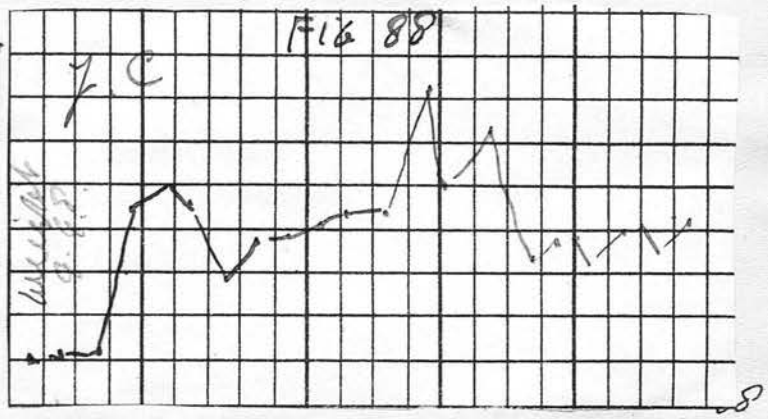
5. T.V.C. 42. 9. 11. '21.

History: Brother died of phthisis. Blood in sputum. Tubercle found in sputum and urine 14 days ago. Cough at night. Yellow expectoration; sleeps badly.

Physical examination: Poor air entry. Nothing to detect in physical signs as denoting activity.

Laryngologist's report: "ulceration of epiglottis in filtration arytenoids."

Began treatment with T.A.F. 0001 and proceeded to 0002 0003 and so on. After a few doses blood disappeared from sputum, and gained weight. Treated up to .15.



Result: Improved rapidly at first, but later the larynx got worse and he had trouble with his bladder. Advised to go to the country. I have not heard from him since, but the prognosis was very bad. FIG.82.

6. G.B. 28. 25. 2 '21.

History: Out patient Brompton three months last year. T.B. in sputum. 3 months in sanatorium. One hemorrhage.

Physical examination: Increased V.R. right apex and also base. B.P. 125. Hb 80%. Clots in 9 minutes.

Treated with P.T.O., commencing with 001; practically reactionless. Then P.T. and T.A.F. up to .1.

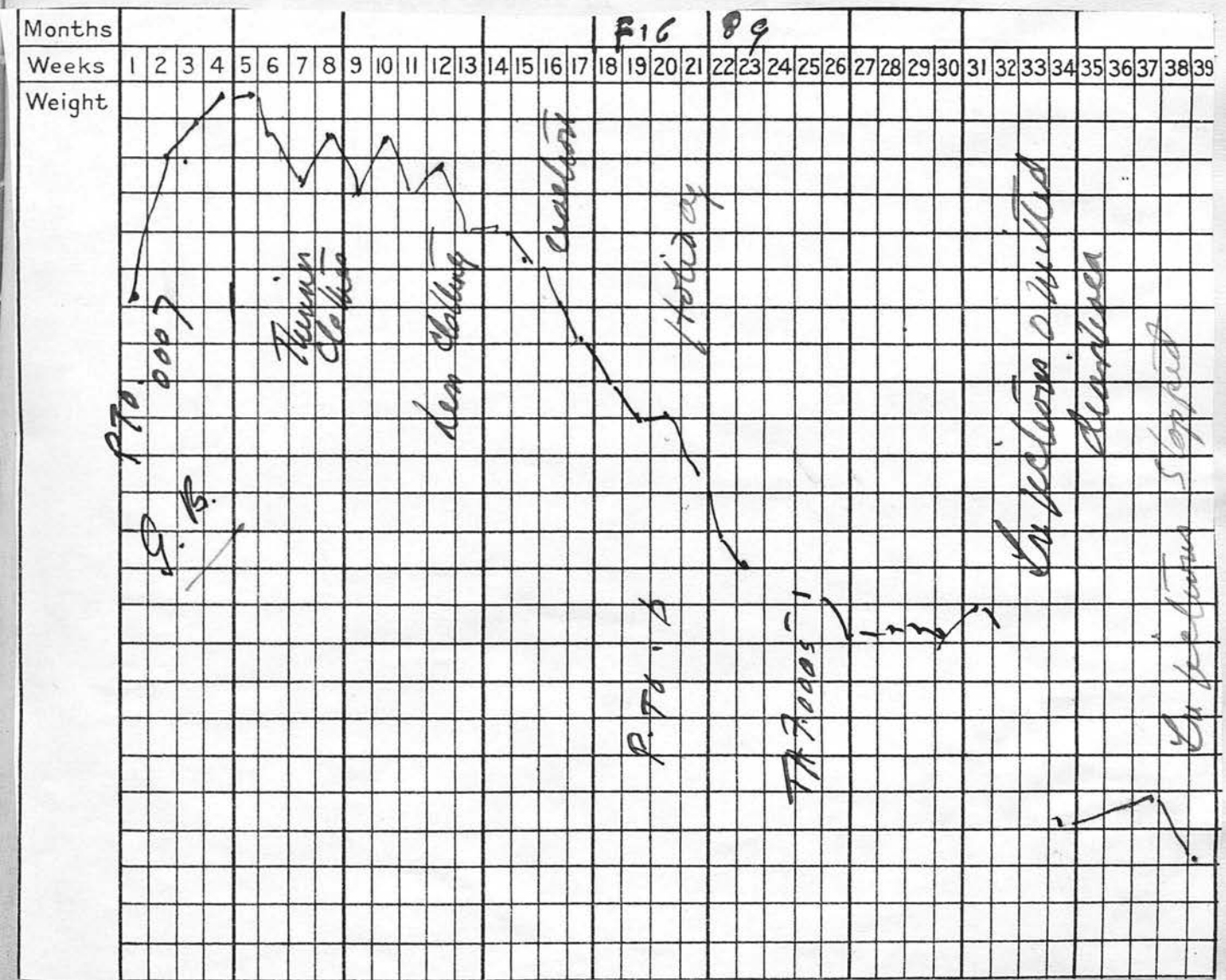
Result: Did well for a while, but later lost weight rapidly. He has had a severe hemorrhage and has been confined to bed for a long time.

Did Tuberculin do harm in this case? I doubt it, for the following reasons: 1. There were no reactions to speak of, and the case was a febrile. 2. There was a distinct improvement for 18 weeks. 3. He went to the bad on his holiday

in the New Forest, in the pouring rain. 4. The trouble was digestive; he was constantly getting indigestion and not absorbing his food.

On the other hand, to maintain that Tuberculin helped him is futile. Were I treating such a case again I should omit treatment whilst he was losing weight and only commence if, and when the weight became stable.

FIG. ~~83~~ 89



Hospital Cases.

1. May W. 12. 30. 11. '22.

History: Mother tubercular. Constant colds.

Physical examination: A few crepitations left apex posteriorly. Expiration prolonged.

X ray: A slight amount of fibroses radiating from the root; otherwise normal.

Diagnosis on general principles as a slight favourable case.

~~——~~ tested.

Started with T.A.F. 0002; doubled; no reaction till 005. Repeated, gave a reaction to 100 and local reaction. Dropped to .0001 and worked up to .04 without reaction. Occasional colds during treatment, so gave a catarrhal vaccine along with T.A.F. Not able to go further as child being sent to boarding-school.

Result: Gained 4 lbs. Much better in herself. No colds.

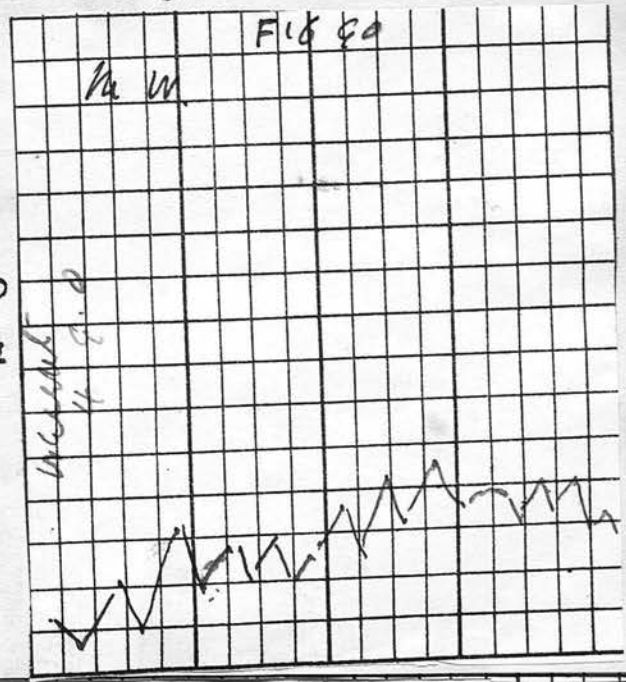


FIG. 84.

2. E.P. 58. 15. 3. '22.

Asthmatic for years each night. Bronchitis. Yellow expectoration. Lost weight.

Physical examination: Marked emphysema. B.P. 160.

X ray: Enlarged hilus glands radiating fibrosis into upper halves of lungs, most marked on right. Heart greatly increased in transverse diameter and appears to be "sitting down" on the diaphram.

Appearances suggest old T.B. possibly still active.

Commenced treatment with T.A.F. .00001 and continued with cautiously increased doses up to 1. cc T.A.F..

Treatment entirely reactionless.

Result: Asthma entirely gone; only slight catarrh in morning. Gained 1 lb in weight.

X ray appearances at end of course have much improved since last report. Do not now suggest activity.

The weight chart is of little interest and is not attached.

A most satisfactory result in every way.

3. A.P. 28. 26. 5. '21.

History: Father's sister asthmatic. Asthma 10 years ago increasing in severity.

Physical examination: A few vales about both apices anteriorly.

X ray report: Hilus shadows enlarged, bands up towards, and apparently into, apices, which appear cloudy.

Started treatment with T.A.F. 00005 and increased fairly rapidly to T.A.F. 1. cc.

Result: Stated felt much better at end of course. Had an attack of asthma three months later.

4. Mrs S. 38. 1. 5. '22.

History: Mother died phthisis. Child T.B. Pains chest for a year. Cough.

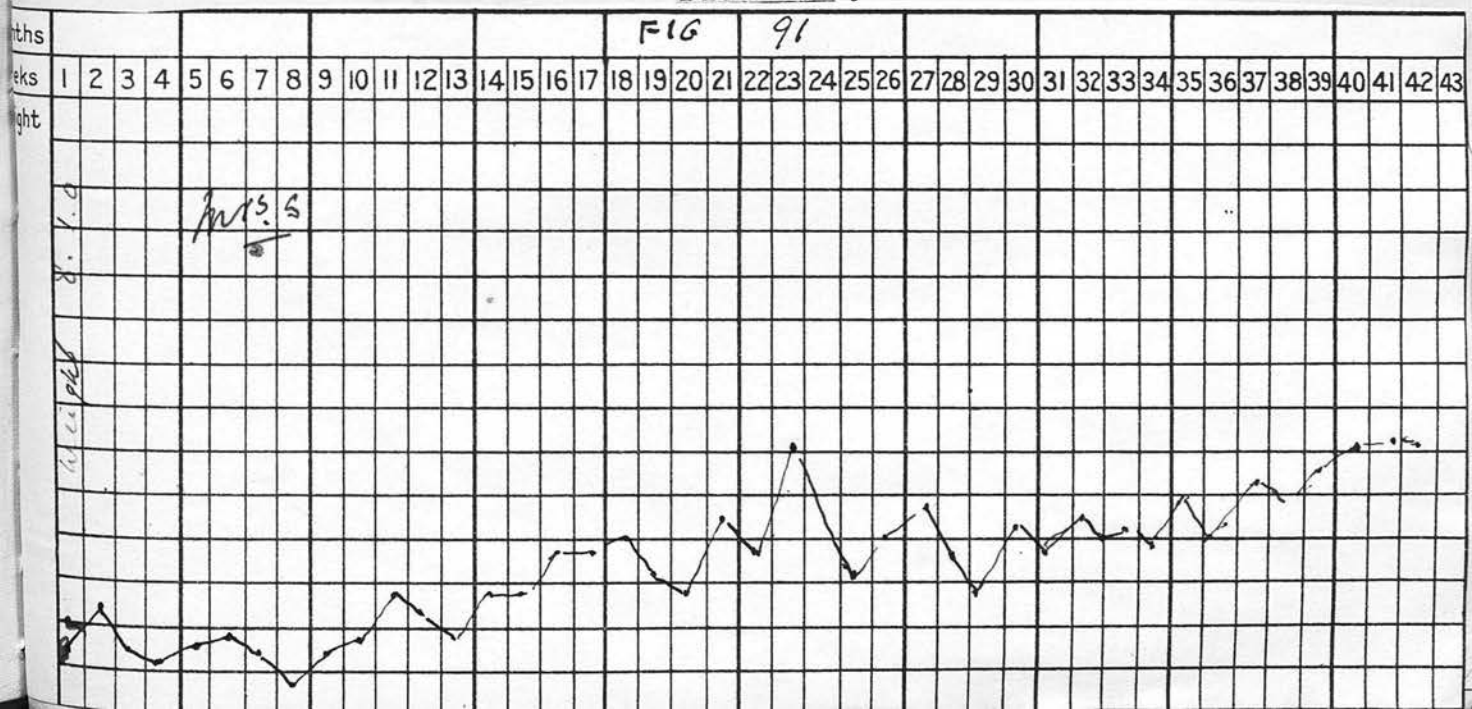
Physical examination: No definite signs in lungs. B.P. 170. Cutaneous reaction reacts to 1 - 10 O.T. ? 1 in 100.

X ray: Fibrous right lung, otherwise no abnormal shadows. Commenced treatment with T.A.F. 00005, continued up to 1. cc. Practically no reactions.

Result: Gained 5 lbs 6 ozs. States she felt absolutely different in every way.

X ray at end: Base of right lung clearer.

FIG. ~~85.~~ 91



5. Mrs W. 45. First seen June 1920.

History: Colds for years. Asthma. Lost weight. Appetite poor.

Physical examination: Very poor air entry right apex. Some dullness. Weight 7. 7. 14. p. 100.

X ray: Heavy root shadows and a good deal of radiating fibrosis. Appearances not characteristic.

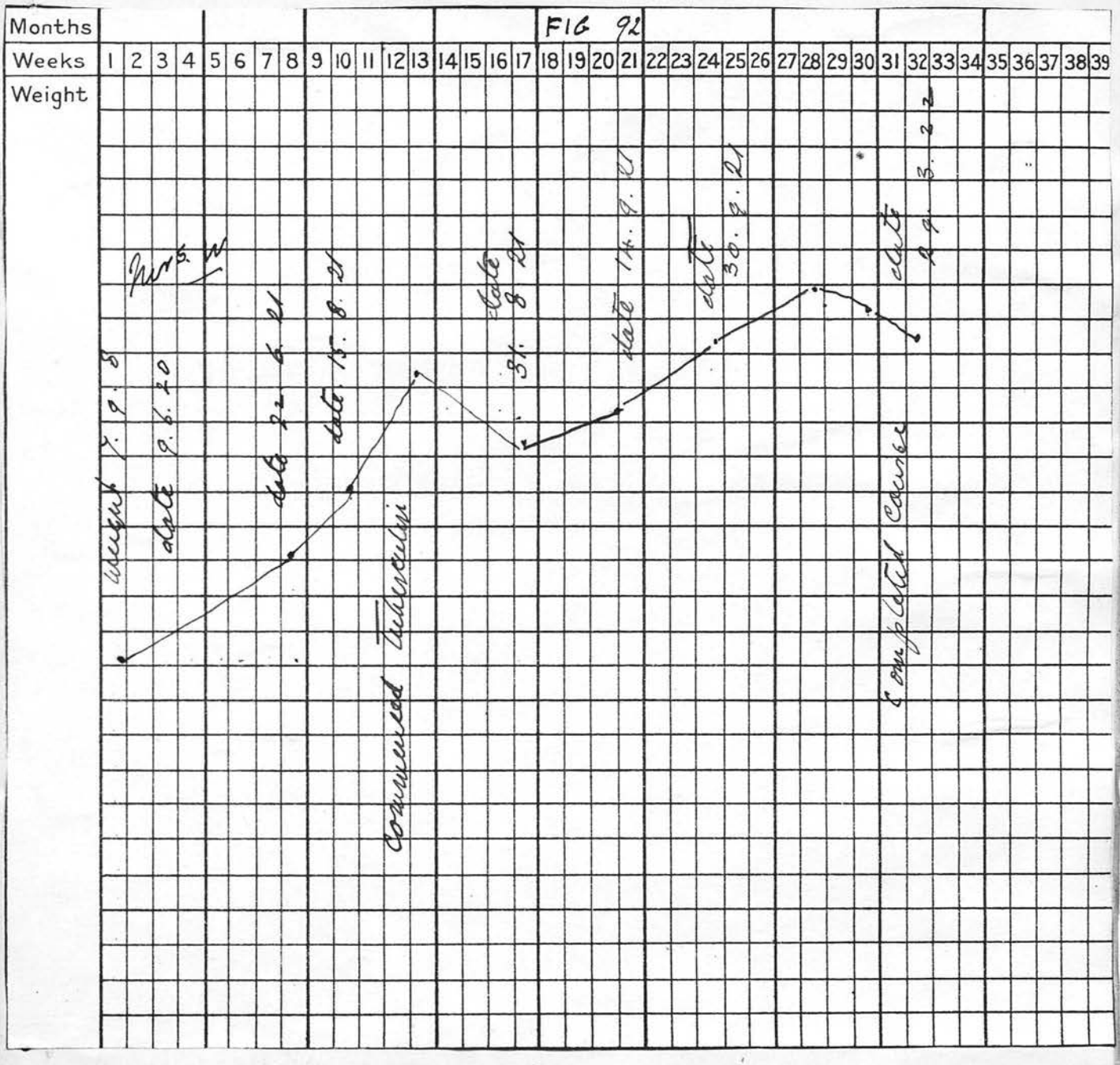
Reacted to 1 in 10 O.T. (cutaneous). Commenced Tuberculin August '21, as not improving.

As there was only a reaction of 1 in 10 commenced with T.A.F. 001 and increased rapidly up to .8 with slight reactions, but never over ~~1~~ 99 .4.

Result: Gained 4 lbs. Asthma and colds apparently cured.

There is no question that this woman did better on Tuberculin than on ordinary treatment which was tried for a year without appreciable benefit.

I consider that I increased the doses too rapidly. In my experience asthma cases do much better with very gradually increasing doses, if you overdose you are apt to bring on an attack.



92

FIG. ~~86~~.

Mrs W.

6. C.M. 35.

Attending West End Hospital for Nervous Diseases.

History: Lost weight; no energy; very neurasthenic.

Nothing to detect in lungs.

Reacted to T.A.F. 008.

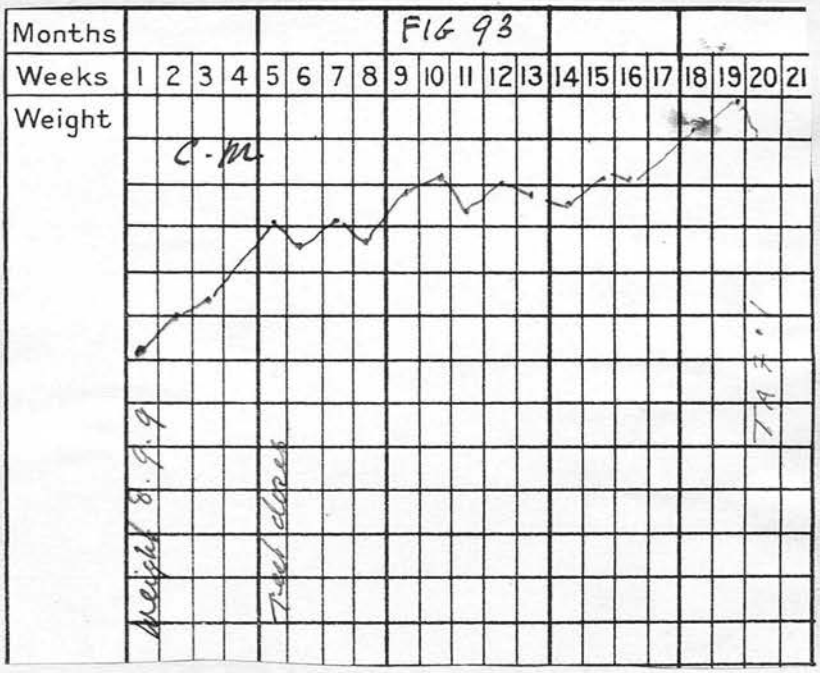
Commenced treatment with T.A.F. 0001, treated up to .1

No reactions.

Result: Very much improved. After this did not attend regularly and dropped back to 8. 11. 0.

93

FIG. 87.



His weight chart is interesting as showing the gain on large test doses.

7. Marjorie W. 22. 1922.

Hisotry: Rheumatoid arthritis in finger joints and pain for years.

Began treating with a detoxicated rheumatic vaccine containing Rheumaticus streptococcus pyogenes Strepl. foxcalis and B. coli.

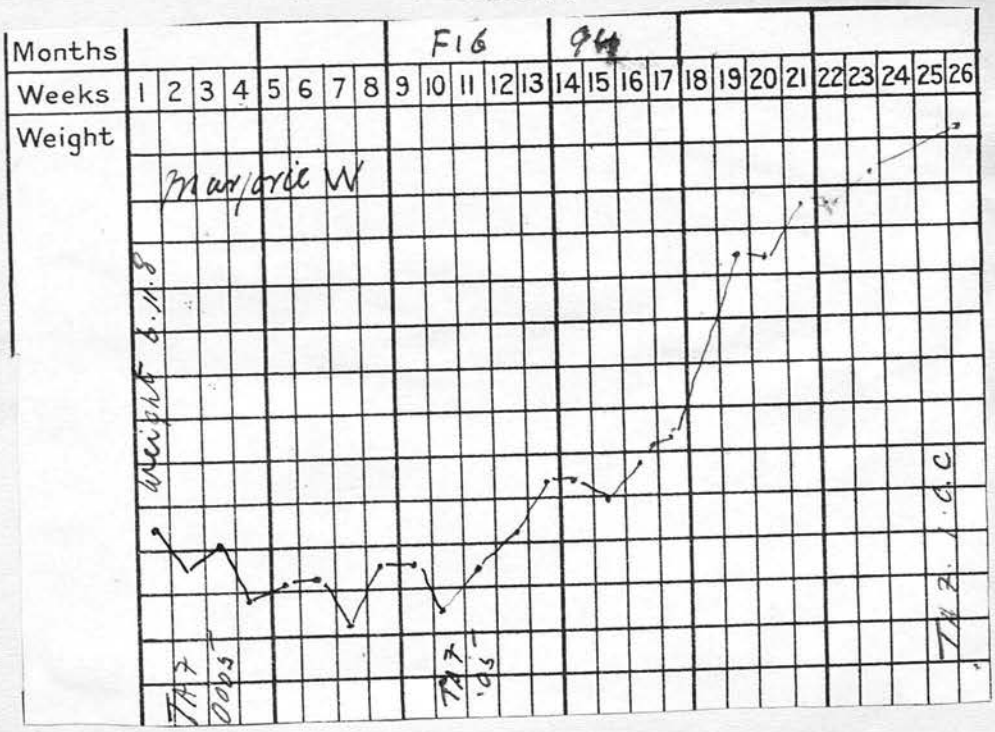
Treatment continued for 3 months without improvement.

I suspected T.B. so gave her T.A.F. 00005 T.A.F. Arm swelled and there was pain in joints.

Consequently I discontinued the Rheumatic vaccine and treated with T.A.F. As soon as I got to T.A.F. 01 she began to increase rapidly in weight. Treated up to 1. cc.

Result: Gained 9 lbs. Feels very much better. Much less swelling in joints.

Saw three months later. Pain less. Health very good. Still a little swelling on one joint (finger).



94
FIG. ~~88~~.

Cases Which Did Not React to Tuberculin Test.

With regard to a positive reaction doubts may be thrown on its value, but of the value of a negative result there is no question, provided, of course, a test is not made on those who are obviously very ill, and who in consequence are too much below par to react at all.

The value of the negative test is that it puts out of court the treatment with Tuberculin, for in those who do not react to test doses Tuberculin is powerless for good or evil.

Below I have noted down briefly a description of the symptoms and signs of a few cases who have not reacted to Tuberculin. I could cite more, but there seems to be no special object in doing so.

1. W.S. aged 12. History: Father and mother reacted to Tuberculin. Treated with benefit. Tired. Enlarged glands neck. Stomach dilated. B.P. 110. p. 90. Hb. 65% ?? left apex.

2. T.B. 42. Chest trouble 2½ years. In "Victoria Park" 3 months. Out of breath. Sleepless. Lost weight. Rhonchi all over chest. Emphysema.

---

3. Mrs B. 29. Tired; nervous. Influenza a year ago. Emaciated. B.P. 130. Hb 80% p. 80. Nothing to detect in lungs.

---

4. Alice B. 25. Both brothers tubercular. Auricular febrillation. Very thin. Eventually died heart failure.

---

5. Rex C. 5. Nervous little boy. Thin. Nothing in chest.

---

6. H.F. 18. Coughs; colds. B.P. 140. Nothing to detect.

---

7. Miss E.C. 18. Cough. Pain both sides. Got thinner. Off food. ? friction right apex. Crepitations both bases. Saw six months later, quite fit.

---

8. Olive G. 4. Mother has T.B. in sputum. Cough each winter. Glands enlarged in neck. Harsh breathing right base.

---

9. R.G. 23. Ulcer Pharynx. Specific. Negative Wassermann.

---

10. Winifred H. 6. Mother tubercular. Constant colds. Adenoids and tonsils removed at Gt. Ormond Street Hospital. Glands neck enlarged. Suspicious harsh breathing right supra scapular region.

Colds treated with a detoxicated catarrhal vaccine.

A few months later said to be quite well.

---

11. Doris H. 7. School doctor thought T.B. Examined by X rays at Shadwell Hospital. Was told shadows pointed to T.B. Anaemic; itritable. Saw a year later, very well.

---

12. Ethel M. 3. Swelling back of left knee for three months (apparently a Bursar). Since whooping cough 4 months ago never fit. Very thin. Nothing abnormal to be detected in lungs.

---

13. E.B.L. 27. Nervous breakdown. Sleeps badly. Indigestion. Liver enlarged.

---

14. Alfred B. 4. Pain right iliac dorsa. Tonsils enlarged. Glands neck enlarged. ? friction right apex.

---

15. Ronald N. 4 years. Enlarged glands neck since a baby. Bad family history.

---

16. Marjorie S. 8. Coughs and colds each winter. Nothing to detect in lungs.

---

17. George S. 7. Mother tubercular. Losing weight. Night sweats. Adenoids. Tubercular Scaphoid. Diagnosed at Guy's Hospital as Kohler's disease.

---

18. Mrs E.S. 28. Cough 3 years. Asthmatic. Lost weight. No suspicious signs in lungs. Very much improved on autogenous vaccine.

---

19. Mrs L.E.S. 43. Asthma. Cough morning and evening. Mother died of phthisis. Frequency of Micturition. Harsh breathing right apex.

---

20. Miss G.T. 21. Enlarged glands neck. Bad history both sides of family.

---

21. C.R.W. 42. Diabetes. Very thin. No signs in lungs.

---

22. Mrs W. 37. Pain in back. Night sweats. Increased V. fremitus right supra acapulor region.

---

23. R.W. 50. Indigestion. Cough at night. Increased vocal resonance and fremitus right apex.

---

24. J.P. 53. Invalided from Army with debility. Night sweats. Cough. Harsh breathing right apex.

STATISTICS.

Statistics in a Thesis of this type seem to be of very little value for the following reasons:

1. The number of cases under review is insufficient.
2. The cases that have been fully treated are bound to show a predominance of success for if cases are doing badly under Tuberculin, you discontinue the treatment, and the more experienced you become the more you are likely to do so.

It appears to be likely that in the future there will be more and more a tendency to select cases, but until we have a more accurate knowledge of how Tuberculin acts, and the metabolic changes that occur in tuberculosis, it is impossible to dogmatise.

It may, however, be of sufficient interest to summarize my results.

Of the 15 Hypersensitive Cases those reacting to .0005 or under -

7 were discharged apparently well.

7 were decidedly improved.

1 was worse.

Of the Sensitive Cases:

a. Those reacting to .101. 12 cases.

8 were discharged apparently well.

3 were improved.

1 was worse.

b. Those reacting to .002. 14 cases.

10. were discharged apparently well.

4 were improved.

Subsensitive 003 and Over.

21 cases.

12 were discharged apparently well.

8 were improved.

1 there was no definite change.

Miscellaneous Cases.

9 cases.

4 were discharged apparently well.

3 improved.

1 no change.

1 died a year later.

Cases with T.B. in Sputum.

6 cases.

1 improved (apparently well).

1 no change.

4 worse.

Hospital Cases.

8 cases.

2 apparently cured.

6 improved.

Out of 85 cases here recorded

43 were discharged apparently well.

33 decidedly improved.

3 there was no change.

6 worse.

If looked at in this way it would give the appearance that Tuberculin is a cure for tuberculosis, but I am very far from trying to prove that. For example, I have had poor results in open tuberculosis and I now employ Tuberculin with extreme caution in these cases.

In the slight cases accompanied with marked toxaemia I have had excellent results and it seems to me that more benefit is derived by early diagnosis of cases, and realising nature's danger signals, than by attempting to treat advanced tuberculosis with Tuberculin, but that even in these cases one is justufied in giving it a trial, observing the greatest caution.

CONCLUSION.

I have come to the following conclusions regarding Tuberculin.

1. That Sahli is right in saying that at present there does not seem to be a great difference, except in degree, between the various Tuberculins, and that more good is obtained by keeping to one Tuberculin and improving one's technique, than by chopping and changing from one brand to another. I myself have certainly had better results since I have used T.A.F. and T.A.F. only, than I used to get when changing from P.T.O. to P.T. and then on to O.T. as Wilkinson at one time advocated.

2. That the Lysin Theory of the Action of Tuberculin, which is that which Sahli believes in, appears to be the most feasible of all theories, for reasons given in a former section.

3. That Sahli's reactionless method is undoubtedly the best, when feasible.

4. That rapidly pushed test doses should not be employed, A modified series of test doses beginning with, say, .0001 T.A.F. and noticing the effect of each increasing dose, is quite sufficient to confirm a diagnosis which can, to a great extent, be made by other methods.

5. That these tests, whether they be cutaneous, or subcutaneous, are not tests of activity, but rather of hypersensitivity to Tuberculin.

6. That the great majority of people will react to Tuberculin probably because they have a focus, too small for detection, in the body, and that unless one realises this one would be treating practically healthy people with Tuberculin quite unnecessarily, simply because they react to Tuberculin. That the real signs of activity are the symptoms and that if these disappear under Tuberculin Therapy then credit must be given to the remedy.

7. That patients may be divided roughly into 3 classes. The Hypersensitive; the Sensitive; and the Subsensitive, and that a different line of treatment must be followed in each class.

8. That Hypersensitiveness is by no means an unfavourable sign. It often points to a good resisting power.

9. That it is in the mild, early stages of tubercle that Tuberculin does so much good. Without Tuberculin these cases would be diagnosed something entirely different, such as dyspepsia, rheumatism, neurasthenia.

10. That in advanced cases it does little, or no, good.

11. But that even in these cases one is justified in trying it, for it is obvious that no other method holds out much hope.

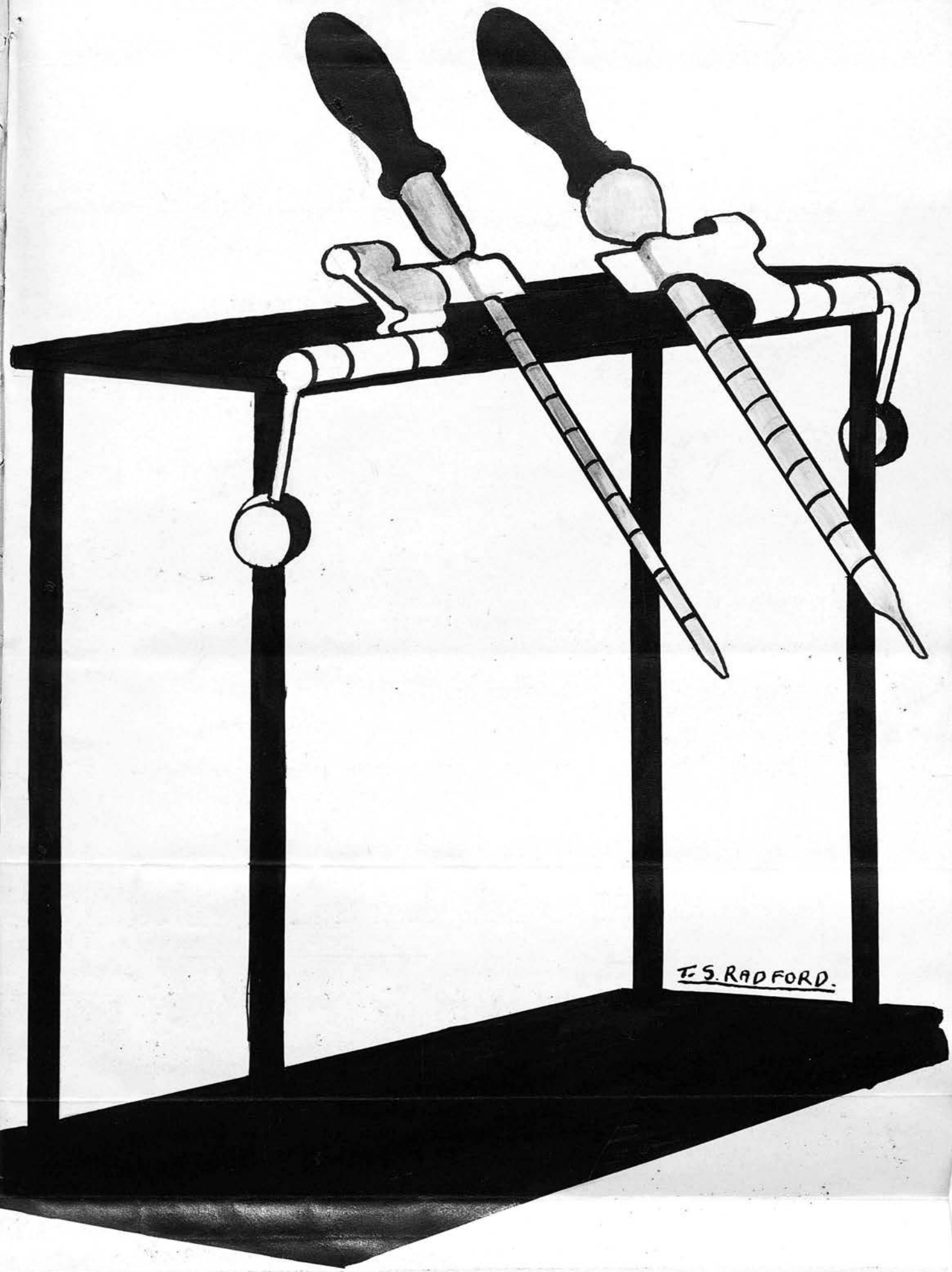
12. That no one should attempt to treat tuberculosis with Tuberculin unless they have had a long course of training under an expert and have studied the theory as well as the practice of Tuberculin. In other words, they should know what they are doing.

13. That mixed infections should be dealt with by means of other vaccines.

14. Lastly, that Tuberculin has a definite position in our attack on tuberculosis, and that this position will become stronger the more we realise its limitations, and keep the treatment as far as possible in the hands of those who have made a study of the problem.

AUTHORITIES CONSULTED.

1. Bandelier and Roepke -
   Tuberculin in Diagnosis and Treatment.
2. Sahli's Tuberculin Therapy.
3. Cochrane and Sprawson's Guide to the Use of Tuberculin.
4. Paterson: Auto Innoculation in Pulmonary Tuberculosis.
5. Camae Wilkinson: Tuberculin Treatment of Consumption.



Author's apparatus for making dilutions of Tuberculin in pipettes fixed on suitable stand.